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=> d his

     (FILE 'HOME' ENTERED AT 06:59:52 ON 08 APR 2000)
               SET COST OFF
               SET AUHELP OFF

     FILE 'REGISTRY' ENTERED AT 07:00:06 ON 08 APR 2000
               E HYALURONIC ACID/CN
L1             1 S E3
               E HYALURONIC ACID, SODIUM SALT/CN
L2             1 S E3

     FILE 'MEDLINE' ENTERED AT 07:00:38 ON 08 APR 2000
L3          4677 S L1 OR L2
L4          6287 S HYALURONIC ACID/CT,CN
L5          6287 S L3,L4
L6          8881 S HYALURONIC ACID OR (NA OR SODIUM)()HYALURON? OR HYALURONATE O
L7             6 S (NA OR SODIUM)()HYALURONIC ACID
L8          8881 S L5-L7
L9            47 S L8 AND (MAST CELLS+NT)/CT
L10           33 S L8 AND (HEMATOPOIETIC SYSTEM+NT)/CT
L11           23 S L8 AND (HEMATOPOIESIS+NT)/CT
L12            0 S L8 AND (HEMATOPOIETIC STEM CELL TRANSPLANTATION+NT)/CT
L13            0 S L8 AND (HEMATOPOIETIC STEM CELL MOBILIZATION+NT)/CT
L14           13 S L8 AND (HEMATOPOIETIC CELL GROWTH FACTORS+NT)/CT
L15            2 S L8 AND (HEMATOPOIETIC CELL GROWTH FACTORS)/CT,CN
L16            2 S L8 AND (RECEPTORS, COLONY-STIMULATING FACTOR+NT)/CT
L17            1 S L8 AND (RECEPTORS, COLONY-STIMULATING FACTOR)/CT,CN
L18            7 S L8 AND (DENDRITIC CELLS+NT)/CT
L19            2 S L8 AND (STEM CELL FACTOR+NT)/CT
L20            3 S L8 AND (STEM CELL FACTOR)/CT,CN
L21          662 S L8 AND STEM CELLS+NT/CT
L22           33 S L8 AND (ERYTHROCYTES+NT)/CT
L23            2 S L8 AND (BLOOD VOLUME+NT)/CT
L24           11 S L8 AND (ERYTHROCYTE COUNT+NT OR ERYTHROCYTE AGGREGATION+NT OR
L25       100186 S STEM CELLS+NT/CT
L26          232 S L25/MAJ AND L21
L27          356 S L9-L20,L22-L24,L26
L28          300 S L27 AND PY<=1996
               E PILARSKI L/AU
L29          113 S E3,E4
L30            2 S L27 AND L29
L31            9 S L29 AND L8
L32            7 S L31 NOT L30
L33            9 S L30-L32
L34           70 S L28 NOT AB/FA
L35            1 S L34 AND (WOUND HEALING)/CT
L36          275 S L8 AND OLDMEDLINE/FS
L37           13 S L36 AND (ERYTHROCYT? OR HEMOGLOBLIN OR MAST CELL OR BLOOD PIC
L38            4 S L37 AND (EXPLOSION OR HEXOSAMINE# OR HEMOGLOBIN)/TI
L39          229 S L28 NOT L29-L38
L40         3276 S L4/MAJ
L41           78 S L39 AND L40
L42         1365 S ((HYALURONIC ACID)(L)(PD OR AD OR TU))/CT
L43           26 S L42 AND L39
L44           13 S L40 AND L43
L45           27 S L33,L35,L38,L44
L46           13 S L43 NOT L45
L47           40 S L45,L46

=> fil reg
FILE 'REGISTRY' ENTERED AT 07:33:19 ON 08 APR 2000
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CM1 1E01 Tel: 308-4498

STRUCTURE FILE UPDATES: 7 APR 2000 HIGHEST RN 261382-10-9
DICTIONARY FILE UPDATES: 7 APR 2000 HIGHEST RN 261382-10-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN 9004-61-9 REGISTRY
CN **Hyaluronic acid (8CI, 9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Artz
CN Hyaluronan
CN Luronit
CN Mucoitin
DR 9039-38-7, 37243-73-5, 29382-75-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
6974 REFERENCES IN FILE CA (1967 TO DATE)
513 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6976 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:214676

REFERENCE 2: 132:212754

REFERENCE 3: 132:212710

REFERENCE 4: 132:212700

REFERENCE 5: 132:212680

REFERENCE 6: 132:212534

REFERENCE 7: 132:212511

REFERENCE 8: 132:208041

REFERENCE 9: 132:206656

REFERENCE 10: 132:206236

=> d ide can l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN 9067-32-7 REGISTRY
CN **Hyaluronic acid, sodium salt (9CI)** (CA INDEX NAME)

OTHER NAMES:
CN Bio Hyaluro 12
CN HA-Q
CN Healon
CN Healon (polysaccharide)
CN Hyalgan
CN Hyladerm
CN NIDELON
CN NRD 101
CN SI 4402
CN SL 1010
CN SLM 10
CN Sodium hyaluronate
CN SPH
DR 34448-35-6
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1013 REFERENCES IN FILE CA (1967 TO DATE)
39 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1014 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:212754

REFERENCE 2: 132:212708

REFERENCE 3: 132:203110

REFERENCE 4: 132:198870

REFERENCE 5: 132:185482

REFERENCE 6: 132:179896

REFERENCE 7: 132:153570

REFERENCE 8: 132:153249

REFERENCE 9: 132:139035

REFERENCE 10: 132:132340

=> fil medline
FILE 'MEDLINE' ENTERED AT 07:33:48 ON 08 APR 2000

FILE LAST UPDATED: 7 APR 2000 (20000407/UP). FILE COVERS 1960 TO DATE.

MEDLINE has been reloaded to reflect the annual MeSH changes made by the National Library of Medicine for 2000. Enter HELP RLOAD for details.

OLDMEDLINE, data from 1960 through 1965 from the Cumulated Index Medicus (CIM), has been added to MEDLINE. See HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all tot l47

L47 ANSWER 1 OF 40 MEDLINE
AN 2000075380 MEDLINE
DN 20075380
TI Beta1-integrins control spontaneous adhesion and motility of human progenitor thymocytes and regulate differentiation-dependent expression of the receptor for **hyaluronan**-mediated motility.
AU Gares S L; **Pilarski L M**
CS Department of Oncology, University of Alberta and Cross Cancer Institute, Edmonton, Alta, Canada.
SO SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1999 Dec) 50 (6) 626-34.
Journal code: UCW. ISSN: 0300-9475.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200003
EW 20000303
AB The functions of the receptor for **hyaluronan**-mediated motility (RHAMM) and beta1-integrin in adhesion and motility were analysed for human progenitor multinegative (CD3- 4- 8- 19-) thymocytes (MN Thy). Both alpha4beta1- and alpha5beta1-integrins are expressed by MN Thy, but only alpha4beta1 mediates fibronectin (FN)-dependent adhesion and motility. Freshly isolated MN Thy lack expression of RHAMM and their motility is RHAMM independent. Prolonged surface expression of RHAMM on MN Thy is dependent upon FN. RHAMM expression, which occurs prior to surface expression of CD3/T-cell receptor (TCR), was found to be inhibited by cross-linking of alpha4-, alpha5- and beta1-integrins, as was the prolonged FN-dependent phase of RHAMM expression. To confirm that RHAMM expression had been down-regulated rather than rendered cryptic by treatment with immobilized anti-integrin monoclonal antibody (MoAb), RHAMM mRNA levels were analysed. Transcription of RHAMM was decreased 7-12-fold by treatment with immobilized anti-alpha4 or anti-alpha5, and twofold by anti-beta1. Prior to expression of CD3/TCR and RHAMM, alpha4beta1 regulates migratory behaviour. After MN Thy differentiate to acquire CD3/TCR in vitro or in vivo, their motility becomes dependent upon both RHAMM and beta1-integrins. Integrins play a direct role in FN-dependent, RHAMM-independent motility of MN Thy, and an indirect role in RHAMM-dependent motility. This work shows that beta1-integrins are primary mediators and regulators of fundamental cell behaviours required during migratory phases of T-cell differentiation that occur prior to the expression of CD3/TCR.
CT Check Tags: Human; Support, Non-U.S. Gov't
Antibodies, Monoclonal: PD, pharmacology
*Antigens, CD29: PH, physiology
*Antigens, CD44: BI, biosynthesis
Antigens, CD44: GE, genetics
Antigens, CD44: IM, immunology
Antigens, Differentiation, T-Lymphocyte: AN, analysis
Cell Adhesion: PH, physiology
Cell Differentiation: GE, genetics
Cell Movement: DE, drug effects
Cell Movement: PH, physiology
Child
Child, Preschool
*Extracellular Matrix Proteins: BI, biosynthesis
Extracellular Matrix Proteins: GE, genetics
Extracellular Matrix Proteins: IM, immunology
Fibronectins: PH, physiology
Gene Expression Regulation, Developmental: DE, drug effects
***Hyaluronic Acid: PD, pharmacology**
Infant
Infant, Newborn
*Integrins: PH, physiology

*Receptors, Fibronectin: PH, physiology
*Receptors, Lymphocyte Homing: PH, physiology
RNA, Messenger: BI, biosynthesis
*T-Lymphocytes: CY, cytology
T-Lymphocytes: ME, metabolism
*Thymus Gland: CY, cytology
RN **9004-61-9 (Hyaluronic Acid)**
CN 0 (integrin alpha4beta1); 0 (Antibodies, Monoclonal); 0 (Antigens, CD29); 0 (Antigens, CD44); 0 (Antigens, Differentiation, T-Lymphocyte); 0 (Extracellular Matrix Proteins); 0 (Fibronectins); 0 (Integrins); 0 (Receptors, Fibronectin); 0 (Receptors, Lymphocyte Homing); 0 (RHAMM protein); 0 (RNA, Messenger)

L47 ANSWER 2 OF 40 MEDLINE
AN 1999233653 MEDLINE
DN 99233653
TI Potential role for **hyaluronan** and the **hyaluronan** receptor RHAMM in mobilization and trafficking of hematopoietic progenitor cells.
AU **Pilarski L M**; Pruski E; Wizniak J; Paine D; Seeberger K; Mant M J; Brown C B; Belch A R
CS Departments of Oncology and Medicine, University of Alberta, Cross Cancer Institute, Edmonton, Alberta, Canada.. lpilarsk@gpu.srv.ualberta.ca
SO BLOOD, (1999 May 1) 93 (9) 2918-27.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199907
EW 19990704
AB Although the mechanism(s) underlying mobilization of hematopoietic progenitor cells (HPCs) is unknown, detachment from the bone marrow (BM) microenvironment and motility are likely to play a role. This work analyzes the motile behavior of HPCs and the receptors involved. CD34(+)45(lo/med)Scatterlo/med HPCs from granulocyte colony-stimulating factor (G-CSF)-mobilized blood and mobilized BM were compared with steady-state BM for their ability to bind **hyaluronan** (HA), their expression of the HA receptors RHAMM and CD44, and their motogenic behavior. Although RHAMM and CD44 are expressed by mobilized blood HPCs, function blocking monoclonal antibodies (MoAbs) identified RHAMM as a major HA binding receptor, with a less consistent participation by CD44. Permeabilization of mobilized blood HPCs showed a pool of intracellular (ic) RHAMM and a smaller pool of icCD44. In contrast, steady-state BM HPCs have significantly larger pools of icRHAMM and icCD44. Also, in contrast to mobilized blood HPCs, for steady-state BM HPCs, MoAbs to RHAMM and CD44 act as agonists to upregulate HA binding. The comparison between mobilized and steady-state BM HPCs suggests that G-CSF mobilization is associated with depletion of intracellular stores of HA receptors and modulates HA receptor usage. To confirm that mobilization alters the HA receptor distribution and usage by HPCs, samples of BM were collected at the peak of G-CSF mobilization in parallel with mobilized blood samples. HA receptor distribution of mobilized BM HPCs was closely matched with mobilized blood HPCs and different from steady-state BM HPCs. Mobilized BM HPCs had lower pools of icHA receptors, similar to those of mobilized blood HPCs. Treatment of mobilized BM HPCs with anti-RHAMM MoAb decreased HA binding, in contrast to steady-state BM HPCs. Thus, G-CSF mobilization may stimulate an autocrine stimulatory loop for HPCs in which HA interacts with basal levels of RHAMM and/or CD44 to stimulate receptor recycling. Consistent with this, treatment of HPCs with azide, nystatin, or cytochalasin B increased HA binding, implicating an energy-dependent process involving lipid rafts and the cytoskeleton. Of the sorted HPCs, 66% were adherent and 27% were motile on fibronectin plus HA. HPC adherence was inhibited by MoAbs to beta1 integrin and CD44, but not to RHAMM, whereas HPC motility was inhibited by MoAb to RHAMM and beta1 integrin, but not to CD44. This finding suggests that RHAMM and CD44 play

reciprocal roles in adhesion and motility by HPCs. The G-CSF-associated alterations in RHAMM distribution and the RHAMM-dependent motility of HPCs suggest a potential role for HA and RHAMM in trafficking of HPCs and the possible use of HA as a mobilizing agent in vivo.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't
*Antigens, CD44: PH, physiology
Blood Component Removal
Bone Marrow Cells: CY, cytology
Bone Marrow Cells: PA, pathology
Breast Neoplasms: BL, blood
Breast Neoplasms: PA, pathology
Cell Division
Cell Membrane: PH, physiology
Cell Movement
*Extracellular Matrix Proteins: PH, physiology
Gene Expression Regulation
Hematopoietic Stem Cells: CY, cytology
Hematopoietic Stem Cells: PA, pathology
***Hematopoietic Stem Cells: PH, physiology**
Hyaluronic Acid: GE, genetics
***Hyaluronic Acid: PH, physiology**
Kinetics
Lymphoma: BL, blood
Lymphoma: PA, pathology
Multiple Myeloma: BL, blood
Multiple Myeloma: PA, pathology
Regression Analysis

RN **9004-61-9 (Hyaluronic Acid)**

CN 0 (Antigens, CD44); 0 (Extracellular Matrix Proteins); 0 (RHAMM protein)

L47 ANSWER 3 OF 40 MEDLINE

AN 1999155348 MEDLINE

DN 99155348

TI Overexpression of the receptor for **hyaluronan**-mediated motility (RHAMM) characterizes the malignant clone in multiple myeloma: identification of three distinct RHAMM variants.

AU Crainie M; Belch A R; Mant M J; **Pilarski L M**

CS Departments of Oncology and Medicine, University of Alberta and the Cross Cancer Institute, Edmonton, Canada.

SO BLOOD, (1999 Mar 1) 93 (5) 1684-96.
Journal code: A8G. ISSN: 0006-4971.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 199905

EW 19990503

AB The receptor for **hyaluronan** (HA)-mediated motility (RHAMM) controls motility by malignant cells in myeloma and is abnormally expressed on the surface of most malignant B and plasma cells in blood or bone marrow (BM) of patients with multiple myeloma (MM). RHAMM cDNA was cloned and sequenced from the malignant B and plasma cells comprising the myeloma B lineage hierarchy. Three distinct RHAMM gene products, RHAMMFL, RHAMM-48, and RHAMM-147, were cloned from MM B and plasma cells. RHAMMFL was 99% homologous to the published sequence of RHAMM. RHAMM-48 and RHAMM-147 variants align with RHAMMFL, but are characterized by sequence deletions of 48 bp (16 amino acids [aa]) and 147 bp (49 aa), respectively. The relative frequency of these RHAMM transcripts in MM plasma cells was determined by cloning of reverse-transcriptase polymerase chain reaction (RT-PCR) products amplified from MM plasma cells. Of 115 randomly picked clones, 49% were RHAMMFL, 47% were RHAMM-48, and 4% were RHAMM-147. All of the detected RHAMM variants contain exon 4, which is alternatively spliced in murine RHAMM, and had only a single copy of the exon 8 repeat sequence detected in murine RHAMM. RT-PCR analysis of sorted blood or BM cells from 22 MM patients showed that overexpression of RHAMM variants is characteristic of MM B cells and BM plasma cells in all patients tested.

RHAMM also appeared to be overexpressed in B lymphoma and B-chronic lymphocytic leukemia (CLL) cells. In B cells from normal donors, RHAMMFL was only weakly detectable in resting B cells from five of eight normal donors or in chronically activated B cells from three patients with Crohn's disease. RHAMM-48 was detectable in B cells from one of eight normal donors, but was undetectable in B cells of three donors with Crohn's disease. RHAMM-147 was undetectable in normal and Crohn's disease B cells. In situ RT-PCR was used to determine the number of individual cells with aggregate RHAMM transcripts. For six patients, 29% of BM plasma cells and 12% of MM B cells had detectable RHAMM transcripts, while for five normal donors, only 1. 2% of B cells expressed RHAMM transcripts. This work suggests that RHAMMFL, RHAMM-48, and RHAMM-147 splice variants are overexpressed in MM and other B lymphocyte malignancies relative to resting or in vivo-activated B cells, raising the possibility that RHAMM and its variants may contribute to the malignant process in B-cell malignancies such as lymphoma, CLL, and MM.

CT Check Tags: Human; Support, Non-U.S. Gov't
Antigens, CD44: BI, biosynthesis
*Antigens, CD44: GE, genetics
B-Lymphocytes: ME, metabolism
*B-Lymphocytes: PA, pathology
Base Sequence
Cell Division
Cell Lineage
Extracellular Matrix Proteins: BI, biosynthesis
*Extracellular Matrix Proteins: GE, genetics
*Gene Expression Regulation, Neoplastic
Molecular Sequence Data
*Multiple Myeloma: GE, genetics
Multiple Myeloma: ME, metabolism
*Multiple Myeloma: PA, pathology
Neoplasm Invasiveness
Sequence Alignment
Sequence Deletion
Transcription, Genetic
*Tumor Markers, Biological

CN 0 (Antigens, CD44); 0 (Extracellular Matrix Proteins); 0 (RHAMM protein); 0 (Tumor Markers, Biological)

L47 ANSWER 4 OF 40 MEDLINE
AN 1999065413 MEDLINE
DN 99065413
TI During human thymic development, beta 1 integrins regulate adhesion, motility, and the outcome of RHAMM/**hyaluronan** engagement.
AU Gares S L; Giannakopoulos N; MacNeil D; Faull R J; **Pilarski L M**
CS Department of Oncology and The Cross Cancer Institute, University of Alberta, Edmonton, Canada.
SO JOURNAL OF LEUKOCYTE BIOLOGY, (1998 Dec) 64 (6) 781-90.
Journal code: IWY. ISSN: 0741-5400.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199902
EW 19990204
AB During human thymic differentiation, interactions between fibronectin (Fn)/beta1 integrins and **hyaluronan** (HA)/RHAMM control motility and Fn/beta1 integrins mediate spontaneous Fn-dependent adhesion. Multinegative (MN, CD3-4-8-) thymocytes exhibit strong spontaneous adherence to Fn (75%) that was efficiently inhibited by anti-alpha5beta1 and only weakly inhibited by anti-alpha4beta1. The relatively weak adherence of unfractionated thymocytes to Fn required both alpha4beta1 and alpha5beta1. Video time-lapse microscopy indicates that a subset of thymocytes also undergo spontaneous Fn-dependent motility mediated by alpha5beta1, alpha4beta1, and the HA-receptor RHAMM, but not by CD44. The loss of motility after hyaluronidase treatment of thymocytes indicated

that motility is strongly dependent on HA. Of motile cells, 55% were DP, 19% were DN, and 24% were CD4+SP, but only 1% were CD8+SP. Overall, for MN thymocytes, beta1 integrin mediated Fn-adhesion, but after expression of CD4/CD8, beta1 integrins mediated Fn-dependent motility. Treatment with the activating anti-beta1 mAb QE.2E5 inhibited thymic motility and converted otherwise nonadherent thymocytes to an adherent state. High-avidity interactions via integrins appear to supercede the motogenicity of RHAMM and HA, suggesting that integrin avidity may regulate RHAMM. During thymic development, changes in adhesion or motility appear to be mediated by integrin avidity modulation.

CT Check Tags: Human; Support, Non-U.S. Gov't
Adult
Antibodies, Blocking: PD, pharmacology
*Antigens, CD29: PH, physiology
*Antigens, CD44: PH, physiology
Cell Adhesion: PH, physiology
Cell Differentiation
*Cell Movement: PH, physiology
Child
Child, Preschool
*Extracellular Matrix Proteins: PH, physiology
***Hyaluronic Acid: PH, physiology**
Infant
Infant, Newborn
Integrins: BI, biosynthesis
Receptors, Fibronectin: BI, biosynthesis
Receptors, Fibronectin: IM, immunology
Receptors, Lymphocyte Homing: BI, biosynthesis
Stem Cells: PH, physiology
T-Lymphocyte Subsets: ME, metabolism
T-Lymphocyte Subsets: PH, physiology
Thymus Gland: CY, cytology
*Thymus Gland: GD, growth & development

RN **9004-61-9 (Hyaluronic Acid)**

CN 0 (integrin alpha4beta1); 0 (Antibodies, Blocking); 0 (Antigens, CD29); 0 (Antigens, CD44); 0 (Extracellular Matrix Proteins); 0 (Integrins); 0 (Receptors, Fibronectin); 0 (Receptors, Lymphocyte Homing); 0 (RHAMM protein)

L47 ANSWER 5 OF 40 MEDLINE

AN 97193612 MEDLINE

DN 97193612

TI Adhesion of multiple myeloma peripheral blood B cells to bone marrow fibroblasts: a requirement for CD44 and alpha4beta7.

AU Masellis-Smith A; Belch A R; Mant M J; **Pilarski L M**

CS Department of Oncology, University of Alberta, Edmonton, Canada.

SO CANCER RESEARCH, (1997 Mar 1) 57 (5) 930-6.
Journal code: CNF. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199706

EW 19970601

AB We have earlier described the presence of phenotypically unusual monoclonal B cells within the peripheral blood of multiple myeloma (MM) patients. To determine the biological properties of these B cells as compared to B cells from normal donors, we investigated the potential of CD19+ MM blood B cells to adhere to endothelial cell and bone marrow (BM)-fibroblast monolayers. We find that 30-60% of freshly isolated CD19+ MM blood B cells adhere to endothelial cell monolayers, and 50-80% adhere to BM fibroblast monolayers. The adhesion of MM blood B cells to either monolayer was not increased by in vitro activation, suggesting that these cells were activated in vivo. In contrast, fewer than 10% of CD19+ B cells from peripheral blood of normal donors adhered. Function-blocking monoclonal antibodies (mAbs) were used to determine which adhesion

receptors were involved in CD19+ MM blood B cell interaction with BM fibroblasts. mAbs against very late antigen 4, the beta7-integrin subunit, and CD44, but not mAbs against very late antigen 5 and beta1, inhibited adhesion 61, 50, and 30%, respectively. The lack of inhibition with mAbs against beta1 implicates alpha4beta7 but not alpha4beta1 in adhesion of CD19+ MM blood B cells. To determine the alpha4beta7 ligand that mediated MM blood B cell adhesion, mAbs against vascular cellular adhesion molecule 1 and fibronectin, as well as CS1 and RGD peptides, were used as inhibitors. These were unable to reduce the adhesion of CD19+ MM blood B cells to BM fibroblasts, suggesting that fibronectin and vascular cellular adhesion molecule 1 are not involved in adhesion. Also, adhesion of MM blood B cells to mucosal addressin cell adhesion molecule 1-transfected Chinese hamster ovary cells was not enhanced compared to control-transfected Chinese hamster ovary cells, suggesting that mucosal addressin cell adhesion molecule 1 was not promoting adhesion of these cells. These data implicate CD44:HA interactions, as well as alpha4beta7 and an as yet unidentified ligand in the adhesion of in vivo activated MM blood B cell adhesion to BM fibroblasts. The adhesion properties of MM CD19+ B cells distinguishes them from normal B cells. Although the malignant status of these cells is as yet undefined, their adhesion properties implicate MM blood B cells in migratory spread of the disease.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
*Antigens, CD: PH, physiology
Antigens, CD19: AN, analysis
*Antigens, CD44: PH, physiology
*B-Lymphocytes: CY, cytology
*Bone Marrow: CY, cytology
Cell Adhesion
*Cell Adhesion Molecules: PH, physiology
CHO Cells
*Endothelium, Vascular: CY, cytology
Fibroblasts: CY, cytology
Fibronectins: ME, metabolism
Hamsters
Hyaluronic Acid: PH, physiology
Immunoglobulins: ME, metabolism
*Integrins: PH, physiology
Molecular Sequence Data
Mucoproteins: ME, metabolism
*Multiple Myeloma: PA, pathology
Peptides: CH, chemistry
Protein Binding
Vascular Cell Adhesion Molecule-1: ME, metabolism

RN 143198-26-9 (alpha4 integrin); **9004-61-9 (Hyaluronic Acid)**

CN 0 (integrin beta7); 0 (mucosal addressin cell adhesion molecule-1); 0 (Antigens, CD); 0 (Antigens, CD19); 0 (Antigens, CD44); 0 (Cell Adhesion Molecules); 0 (Fibronectins); 0 (Immunoglobulins); 0 (Integrins); 0 (Mucoproteins); 0 (Peptides); 0 (Vascular Cell Adhesion Molecule-1)

L47 ANSWER 6 OF 40 MEDLINE

AN 96213959 MEDLINE

DN 96213959

TI Effects of **hyaluronic acid** on fibroblast behavior in peritoneal injury.

AU Klein E S; Asculai S S; Ben-Ari G Y

CS The Department of Surgery C, The Chaim Sheba Medical Center, Tel Aviv University, Israel.

SO JOURNAL OF SURGICAL RESEARCH, **(1996 Mar)** 61 (2) 473-6.
Journal code: K7B. ISSN: 0022-4804.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199610

AB The process of intraperitoneal adhesion formation is affected by

macrophages and fibroblasts which are major components of postsurgical peritoneal repair. **Hyaluronic acid** (HA) has been shown to affect cellular behavior. We studied the effects of HA on experimental adhesions in vivo and its in vitro effect on cultured postsurgical macrophages and fibroblasts. Experimental adhesions were facilitated by laparotomy and localized peritoneal controlled trauma in two groups of rats (A, B). Postoperatively, group A received intraperitoneal (ip) treatment by HA (1 mg/kg) for 7 days, and group B, ip saline. The rats were then reoperated upon, and adhesions scored. In vitro studies were performed on postsurgical macrophages and fibroblasts. Fibroblasts were obtained using a single-cell suspension technique by debridement of adhesions. The fibroblasts were cultured for 7 days, and their metabolic activity was assessed by the uptake of [3H]thymidine. Postoperative macrophages were obtained from the peritoneal fluid of the rats operated on, and their effect upon fibroblast [3H]thymidine uptake was studied in mixed cultures. The adhesion score of the HA-treated rats was smaller than the score of the saline-treated group. This observation suggests that ip treatment by HA may decrease adhesion formation in this rat model. [3H]Thymidine uptake by cultured postsurgical fibroblasts was significantly lower in the HA-treated group compared to that of controls. In vitro addition of HA to cultured "saline fibroblast" resulted in a significant decrease in [3H]thymidine uptake, suggesting a direct effect of HA on postsurgical fibroblast metabolism. However, [3H]thymidine uptake by fibroblasts in mixed cultures with macrophages obtained from HA-treated rats was significantly increased. These observations suggest that HA may affect the process of peritoneal healing by direct effect on fibroblast metabolic activity, and indirectly via modification of the macrophage-fibroblast interrelationship.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Adhesions
Cells, Cultured
***Fibroblasts: DE, drug effects**
Fibroblasts: PH, physiology
***Hyaluronic Acid: PD, pharmacology**
*Macrophages: DE, drug effects
*Peritoneal Diseases: PA, pathology
Rats
Rats, Sprague-Dawley
Thymidine: ME, metabolism

RN 50-89-5 (Thymidine); **9004-61-9 (Hyaluronic Acid)**

L47 ANSWER 7 OF 40 MEDLINE
AN 96202513 MEDLINE
DN 96202513
TI **Hyaluronan**-dependent motility of B cells and leukemic plasma cells in blood, but not of bone marrow plasma cells, in multiple myeloma: alternate use of receptor for **hyaluronan**-mediated motility (RHAMM) and CD44.
AU Masellis-Smith A; Belch A R; Mant M J; Turley E A; **Pilarski L M**
CS Department of Oncology, University of Alberta, Edmonton, Canada.
SO BLOOD, (1996 Mar 1) 87 (5) 1891-9.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199609
AB We investigated the ability of blood B cells, bone marrow (BM) plasma cells, and terminal leukemic plasma cells (T-PCL) from patients with multiple myeloma (MM) to migrate on extracellular matrix proteins. **Hyaluronan** (HA), but not collagen type I, collagen type IV, or laminin, promoted migration of MM blood B cells, as determined by time-lapse video microscopy. Between 13% and 20% of MM blood B cells migrated on HA with an average velocity of 19 micron/min, and greater than 75% of MM blood B cells exhibited vigorous cell movement and plasma membrane deformation, as did circulating T-PCL and extraskeletal plasma

cells from patients with MM. In contrast, plasma cells obtained from BM of patients with MM lacked motility on all substrates tested and did not exhibit cell membrane protrusions or cellular deformation. MM blood B cells and MM plasma cells from all sources examined expressed the HA-binding receptors receptor for HA-mediated motility (RHAMM) and CD44. On circulating MM B cells, both RHAMM and CD44 participated in HA-binding, indicating their expression ex vivo in an activated conformation. In contrast, for the majority of BM plasma cells in the majority of patients with MM, expression of RHAMM or CD44 was not accompanied by HA binding. A minority of patients did have HA-binding BM plasma cells, involving both RHAMM and CD44, as evidenced by partial blocking with monoclonal antibodies (MoAbs) to RHAMM or to CD44. Despite HA binding by both RHAMM and CD44, migration of MM blood B cells on HA was inhibited by anti-RHAMM but not by anti-CD44 MoAbs, indicating that RHAMM but not CD44 mediates motility on HA. Thus, circulating B and plasma cells in MM exhibit RHAMM- and HA-dependent motile behavior indicative of migratory potential, while BM plasma cells are sessile. We speculate that a subset(s) of circulating B or plasma cells mediates malignant spread in myeloma.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Antigens, CD44: DE, drug effects
*Antigens, CD44: PH, physiology
*B-Lymphocyte Subsets: DE, drug effects
B-Lymphocyte Subsets: UL, ultrastructure
*Bone Marrow: PA, pathology
Cell Adhesion
Cell Membrane: UL, ultrastructure
*Chemotaxis, Leukocyte: DE, drug effects
Extracellular Matrix Proteins: DE, drug effects
*Extracellular Matrix Proteins: PH, physiology
***Hyaluronic Acid: PD, pharmacology**
Microscopy, Electron, Scanning
*Multiple Myeloma: PA, pathology
Plasma Cells: CL, classification
*Plasma Cells: DE, drug effects
Protein Binding
***Tumor Stem Cells: DE, drug effects**
Tumor Stem Cells: UL, ultrastructure
RN **9004-61-9 (Hyaluronic Acid)**
CN 0 (Antigens, CD44); 0 (Extracellular Matrix Proteins); 0 (RHAMM protein)

L47 ANSWER 8 OF 40 MEDLINE
AN 95300193 MEDLINE
DN 95300193
TI Adherence, proliferation and collagen turnover by human fibroblasts seeded into different types of collagen sponges.
AU Middelkoop E; de Vries H J; Ruuls L; Everts V; Wildevuur C H; Westerhof W
CS Department of Cell Biology and Histology, Academic Medical Center, Amsterdam, The Netherlands..
SO CELL AND TISSUE RESEARCH, **(1995 May)** 280 (2) 447-53.
Journal code: CQD. ISSN: 0302-766X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509
AB We describe an in vitro model that we have used to evaluate dermal substitutes and to obtain data on cell proliferation, the rate of degradation of the dermal equivalent, contractibility and de novo synthesis of collagen. We tested three classes of collagenous materials: (1) reconstituted non-crosslinked collagen, (2) reconstituted collagen that was chemically crosslinked with either glutaraldehyde, aluminium alginate or acetate, and (3) native collagen fibres, with or without other extracellular matrix molecules (elastin hydrolysate, **hyaluronic acid** or fibronectin). The non-crosslinked reconstituted collagen was degraded rapidly by human fibroblasts. The chemically crosslinked materials proved to be cytotoxic. Native collagen fibres were stable. In

the absence of ascorbic acid, the addition of elastin hydrolysate to this type of matrix reduced the rate of collagen degradation. Both elastin hydrolysate and fibronectin partially prevented fibroblast-mediated contraction. **Hyaluronic acid** was only slightly effective in reducing the collagen degradation rate and more fibroblast-mediated contraction of the material was found than for the native collagen fibres with elastin hydrolysate and fibronectin. In the presence of ascorbate, collagen synthesis was enhanced in the native collagen matrix without additions and in the material containing elastin hydrolysate, but not in the material with **hyaluronic acid**. These results are indicative of the suitability of tissue substitutes for in vivo application.

CT Check Tags: Human; Support, Non-U.S. Gov't
Ascorbic Acid: PD, pharmacology
Cell Adhesion
Cell Division
Cells, Cultured
*Collagen
Collagen: DE, drug effects
Collagen: ME, metabolism
Cross-Linking Reagents: PD, pharmacology
Elastin: PD, pharmacology
Extracellular Matrix: ME, metabolism
***Fibroblasts: CY, cytology**
Fibroblasts: ME, metabolism
Fibronectins: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
Microscopy, Electron, Scanning
*Skin, Artificial
*Surgical Sponges
*Tissue Culture: IS, instrumentation

RN 50-81-7 (Ascorbic Acid); **9004-61-9 (Hyaluronic Acid)**; 9007-34-5 (Collagen); 9007-58-3 (Elastin)

CN 0 (Cross-Linking Reagents); 0 (Fibronectins)

L47 ANSWER 9 OF 40 MEDLINE

AN 95221915 MEDLINE

DN 95221915

TI **Hyaluronic acid** enhances cell proliferation during eosinopoiesis through the CD44 surface antigen.

AU Hamann K J; Dowling T L; Neeley S P; Grant J A; Leff A R

CS Department of Medicine, University of Chicago, IL 60637, USA.

NC AI-34566 (NIAID)
AI-32654 (NIAID)
HL-46368 (NHLBI)

SO JOURNAL OF IMMUNOLOGY, **(1995 Apr 15)** 154 (8) 4073-80.
Journal code: IFB. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 199507

AB We examined the effect of **hyaluronic acid** in promoting proliferation of undifferentiated progenitor cells through the CD44 receptor during eosinopoiesis in vitro. Undifferentiated umbilical cord blood cells were purified on the first day to isolate primitive progenitor cells expressing the CD34 hemopoietic surface marker. Culture in wells coated with 100 micrograms/ml **hyaluronic acid** caused a 198 +/- 28.7% augmentation of proliferation of CD34+ progenitor cells at 3 wk ($p < 0.01$). By contrast, concentrations of **hyaluronic acid** > 10 micrograms/ml inhibited proliferation of unfractionated cord blood mononuclear cells. The augmented proliferation of precursor cells caused by **hyaluronic acid** was associated with complete (93.0 +/- 5.12%) differentiation to eosinophil morphology. By contrast, concentrations of **hyaluronic acid** > or = 10 micrograms/ml inhibited eosinophilic differentiation of unfractionated

mononuclear cells. Wright-Giemsa staining demonstrated 95.4 +/- 2.92% eosinophils for CD34+ cells cultured for 3 wk without **hyaluronic acid** (control) and 93.8 +/- 5.11% for CD34+ cells cultured in **hyaluronic acid**-coated wells (100 micrograms/ml); for unfractionated cells, 94.0 +/- 3.02% demonstrated eosinophilic morphology in control wells at 3 wk vs 55.4 +/- 8.34% in **hyaluronic acid**-coated (100 micrograms/ml) wells ($p < 0.05$). Augmented proliferation caused by **hyaluronic acid** was attenuated completely by the anti-CD44 mAbs, 212.3 and IM7.8.1. Pretreatment of CD34+ cells with 5 micrograms/ml 212.3 inhibited the augmented proliferation caused by the optimal concentration of **hyaluronic acid** (100 micrograms/ml) from 260 +/- 39.2% of control growth to 114 +/- 16.4% of control growth ($p = 0.02$). Inhibition was comparable for IM7.8.1. Control mAb (LM2) to the beta 2 integrin subunit CD11b had no effect on proliferation induced by **hyaluronic acid**. We demonstrate that **hyaluronic acid** stimulates the growth of CD34+ selected umbilical cord blood cells into specifically differentiated mature eosinophils. This process is modulated by the CD44 receptor on the progenitor cell population.

CT Check Tags: Human; In Vitro; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigens, CD: ME, metabolism
*Carrier Proteins: PH, physiology
Cell Division: DE, drug effects
Cell Separation
Cells, Cultured
Chondroitin Sulfates: PD, pharmacology
*Eosinophils: CY, cytology
Fetal Blood: CY, cytology
***Hematopoiesis: DE, drug effects**
***Hematopoietic Stem Cells: CY, cytology**
***Hyaluronic Acid: PD, pharmacology**
Hyaluronoglucosaminidase: PD, pharmacology
Interleukin-3: PD, pharmacology
Interleukin-5: PD, pharmacology
*Receptors, Cell Surface: PH, physiology
*Receptors, Lymphocyte Homing: PH, physiology

RN **9004-61-9 (Hyaluronic Acid)**; 9007-28-7 (Chondroitin Sulfates)

CN EC 3.2.1.35 (Hyaluronoglucosaminidase); 0 (Antigens, CD); 0 (Antigens, CD34); 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Interleukin-3); 0 (Interleukin-5); 0 (Receptors, Cell Surface); 0 (Receptors, Lymphocyte Homing)

L47 ANSWER 10 OF 40 MEDLINE

AN 95111345 MEDLINE

DN 95111345

TI RHAMM, a receptor for **hyaluronan**-mediated motility, on normal human lymphocytes, thymocytes and malignant B cells: a mediator in B cell malignancy?.

AU **Pilarski L M**; Masellis-Smith A; Belch A R; Yang B; Savani R C; Turley E A

CS Department of Immunology, University of Alberta, Edmonton, Canada..

SO LEUKEMIA AND LYMPHOMA, (1994 Aug) 14 (5-6) 363-74. Ref: 83
Journal code: BNQ. ISSN: 1042-8194.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 199504

AB RHAMM (Receptor for HA Mediated Motility) is a novel HA receptor that has been linked to regulating cell locomotion and density dependent contact inhibition of fibroblasts, smooth muscle cells, macrophages, lymphocytes, astrocytes and sperm. The ubiquitous expression of RHAMM suggests the existence of multiple isoforms, and indeed, RHAMM is found in various

cellular compartments, namely nuclear, cytosolic, membrane-bound and extracellular. In this review, we emphasize the evolving role of RHAMM in B cell malignancies, and examine the function of RHAMM in T cell development in the thymic microenvironment. Both the motile behaviour of progenitor thymocytes (CD3-CD4-CD8-) and malignant B cells from multiple myeloma (MM), plasma cell leukemia, and hairy cell leukemia was blocked by monoclonal antibodies to RHAMM, suggesting that motility may correlate with increased expression of RHAMM at the cell surface. Interestingly, the soluble form of RHAMM is able to inhibit fibroblast locomotion, and it is likely that a balance between expression of both forms determines, in part the motility of cells. RHAMM appears to play a fundamental role in the immune system and the ability of RHAMM to function as a motility receptor is likely to be due to complex variables including the extent to which soluble RHAMM is secreted. RHAMM expression characterizes circulating monoclonal B cells as abnormal. potentially invasive and/or metastatic components of myeloma and may underlie the malignant behavior of these cells.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*B-Lymphocytes: PH, physiology
*Carrier Proteins: PH, physiology
Cell Communication
Cell Movement
Hyaluronic Acid: ME, metabolism
*Multiple Myeloma: BL, blood
*Receptors, Cell Surface: PH, physiology
*Receptors, Lymphocyte Homing: PH, physiology
*T-Lymphocytes: PH, physiology

RN **9004-61-9 (Hyaluronic Acid)**

CN 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Receptors, Cell Surface); 0 (Receptors, Lymphocyte Homing)

L47 ANSWER 11 OF 40 MEDLINE

AN 95094913 MEDLINE

DN 95094913

TI Plasmodium falciparum: a family of sulphated glycoconjugates disrupts erythrocyte rosettes.

AU Rowe A; Berendt A R; Marsh K; Newbold C I

CS Molecular Parasitology Group, John Radcliffe Hospital, Oxford, United Kingdom.

SO EXPERIMENTAL PARASITOLOGY, **(1994 Dec)** 79 (4) 506-16.
Journal code: EQP. ISSN: 0014-4894.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199503

AB The ability of Plasmodium falciparum-infected erythrocytes to form spontaneous rosettes with uninfected red cells is a parasite adhesion property which has been associated with severe malaria. The mechanism of rosetting remains unknown, but the ability of heparin to disrupt rosettes has been recognised previously. In this paper we show that a group of sulphated glycoconjugates including sulphatide, dextran sulphate, and fucoidan are more effective rosette reversing agents than heparin and are active against both laboratory strains and wild isolates. Other related anionic glycosaminoglycans such as the chondroitin sulphates A, B, and C and **hyaluronic acid** have no effect on rosette formation. This family of sulphated glycoconjugates which are active against rosettes is also known to inhibit sporozoite invasion of hepatocytes and merozoite reinvasion of erythrocytes, suggesting that sulphated glycoconjugate interaction may be an important process in cell adhesion at different stages in the plasmodial life cycle.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Cell Adhesion: DE, drug effects
Chondroitin Sulfates: PD, pharmacology
Dextran Sulfate: PD, pharmacology
Dose-Response Relationship, Drug

***Erythrocytes: PS, parasitology**
*Glycoconjugates: PD, pharmacology
Heparin: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
*Plasmodium falciparum: DE, drug effects
Plasmodium falciparum: ME, metabolism
Polysaccharides: PD, pharmacology
Rosette Formation
Sulfoglycosphingolipids: PD, pharmacology
*Sulfuric Acid Esters: PD, pharmacology
Suramin: PD, pharmacology
RN 145-63-1 (Suramin); **9004-61-9 (Hyaluronic Acid)**; 9005-49-6 (Heparin); 9007-28-7 (Chondroitin Sulfates); 9042-14-2 (Dextran Sulfate); 9072-19-9 (fucoidan)
CN 0 (Glycoconjugates); 0 (Polysaccharides); 0 (Sulfoglycosphingolipids); 0 (Sulfuric Acid Esters)

L47 ANSWER 12 OF 40 MEDLINE
AN 94331694 MEDLINE
DN 94331694
TI [Action of proteoglycans on erythrocytes in circulating blood]. Deistvie proteoglikanov na eritrotsity v tsirkuliruiuschhei krovi.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1993 Mar)** 115 (3) 240-2.
Journal code: A74. ISSN: 0365-9615.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199411
AB Rabbit and mice were injected into the blood stream **sodium hyaluronate** (0.1 mg per 1 g of the body animal) and protein-chondroitin-keratan-sulfate sodium (0.2 mg per 1 g of the body animal) in 0.15 M NaCl solution. It was shown that both proteoglycans in the blood stream the aggregation action on the erythrocytes in the blood stream. The action finished after 24 hours later on the injection of proteoglycans during in which time the circulating the proteoglycans is remove out of the plasma.
CT Check Tags: Animal
Biopolymers
Blood Circulation: DE, drug effects
English Abstract
Erythrocyte Aggregation: DE, drug effects
***Erythrocytes: DE, drug effects**
Hyaluronic Acid: PD, pharmacology
Keratan Sulfate: PD, pharmacology
Mice
Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Rabbits
RN **9004-61-9 (Hyaluronic Acid)**; 9056-36-4 (Keratan Sulfate)
CN 0 (keratan sulfate proteoglycan); 0 (Biopolymers); 0 (Proteochondroitin Sulfates); 0 (Proteoglycans)

L47 ANSWER 13 OF 40 MEDLINE
AN 94246157 MEDLINE
DN 94246157
TI Role of CD44 in the development of natural killer cells from precursors in long-term cultures of mouse bone marrow.
AU Delfino D V; Patrene K D; DeLeo A B; DeLeo R; Herberman R B; Boggs S S
CS Department of Radiation Oncology, University of Pittsburgh School of Medicine, PA 15261.
NC 5-R01-CA55705 (NCI)
SO JOURNAL OF IMMUNOLOGY, **(1994 Jun 1)** 152 (11) 5171-9.
Journal code: IFB. ISSN: 0022-1767.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199408
AB The role of the adhesion molecule CD44 in the development of NK cells was analyzed in a mouse long-term bone marrow culture system. After 4 wk of culture (day 0), recombinant human IL-2 was added and 13 days later the cells generated were shown to have substantial cytotoxic activity against YAC-1 and to be enriched for NK cells, as assessed for NK-1.1 phenotype by flow cytometric analysis. Physical separation between stroma and precursors partially inhibited proliferation and, consequently, a lower number of cytotoxic cells were produced. Similar results were obtained when an anti-CD44 mAb was added together with IL-2 at day 0. The disruption of **hyaluronic acid** (HA), one of the ligands of CD44, by hyaluronidase or the competition for the binding of CD44 by soluble HA added with IL-2 on day 0 inhibited both proliferation and development of cytotoxicity to a greater degree than did anti-CD44. These results indicate that interaction of CD44 with HA plays an important role in the development of pre-NK cells into cytotoxic effector cells.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: IM, immunology
Binding, Competitive
*Bone Marrow: CY, cytology
*Carrier Proteins: PH, physiology
Cells, Cultured
Chondroitin Sulfates: PD, pharmacology
***Hematopoietic Stem Cells: PH, physiology**
Hyaluronic Acid: PD, pharmacology
Hyaluronoglucosaminidase: PD, pharmacology
*Killer Cells, Natural: PH, physiology
Mice
Mice, Inbred C57BL
*Receptors, Cell Surface: PH, physiology
*Receptors, Lymphocyte Homing: PH, physiology
RN **9004-61-9 (Hyaluronic Acid)**; 9007-28-7 (Chondroitin Sulfates)
CN EC 3.2.1.35 (Hyaluronoglucosaminidase); 0 (Antibodies, Monoclonal); 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Receptors, Cell Surface); 0 (Receptors, Lymphocyte Homing)

L47 ANSWER 14 OF 40 MEDLINE
AN 94171837 MEDLINE
DN 94171837
TI Effects of **hyaluronan** on collagen fibrillar matrix contraction by fibroblasts.
AU Huang-Lee L L; Wu J H; Nimni M E
CS Department of Biochemistry, School of Medicine, University of Southern California, Los Angeles..
SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, **(1994 Jan)** 28 (1) 123-32.
Journal code: HJJ. ISSN: 0021-9304.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
AB **Hyaluronan**, found in high concentrations in fetal tissues, appears to have a major role in preventing scar formation in fetal wounds. Nevertheless, its role in inhibiting wound contractures associated with scar formation has not been clearly demonstrated. Our current study evaluated the effects of **hyaluronan** using an in vitro floating collagen fibrillar matrix (CFM) contraction model. The results demonstrated that the contraction of CFM by fibroblasts was significantly reduced when high concentrations (> 1 mg/mL) of **hyaluronan** were present in the media. This phenomenon is unique to **hyaluronan**, because chondroitin sulfate was ineffective in this connection. Fibroblast

migration and proliferation studies indicated that high concentrations of **hyaluronan** stimulated cell migration and had no cytotoxic effects. Some possible mechanisms by which high concentrations of **hyaluronan** reduced CFM contraction by fibroblasts were proposed. Because the viscosity of a **hyaluronan** solution is much greater than that of chondroitin sulfate, and this increases with concentration, we investigated whether this property in itself was an important factor in inhibiting CFM contraction. No direct correlation was found between the viscosity of glycosaminoglycans and their ability to reduce CFM contraction.

CT Check Tags: Animal; Human
Cattle
Cell Division: DE, drug effects
Cell Movement: PH, physiology
Cells, Cultured
Chondroitin Sulfates: PD, pharmacology
*Cicatrix: PC, prevention & control
*Collagen: DE, drug effects
DNA: ME, metabolism
***Fibroblasts: DE, drug effects**
Fibroblasts: UL, ultrastructure
Glycosaminoglycans: CH, chemistry
Glycosaminoglycans: IP, isolation & purification
***Hyaluronic Acid: PD, pharmacology**
Viscosity

RN **9004-61-9 (Hyaluronic Acid)**; 9007-28-7 (Chondroitin Sulfates); 9007-34-5 (Collagen); 9007-49-2 (DNA)

CN 0 (Glycosaminoglycans)

L47 ANSWER 15 OF 40 MEDLINE

AN 93256549 MEDLINE

DN 93256549

TI Rheological effects of the presence of **hyaluronic acid** in the extracellular media of differentiated 3T3-L1 preadipocyte cultures.

AU Calvo J C; Gandjbakhche A H; Nossal R; Hascall V C; Yanagishita M

CS Proteoglycan Chemistry Section, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland 20892..

SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, **(1993 May)** 302 (2) 468-75.
Journal code: 6SK. ISSN: 0003-9861.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199308

AB The viscoelastic properties of culture medium obtained from confluent 3T3-L1 preadipocytes, after differentiation with isobutyl-methylxanthine and dexamethasone, were studied with a rotational Couette viscometer. In close association with adipocyte differentiation, the culture medium showed gel-like properties, in concert with an increase in viscosity. This behavior vanishes after digestion by Streptomyces hyaluronidase or chondroitinase ABC, but not after application of collagenase, pronase, trypsin, DNase, or neuraminidase, or by treatment with EDTA or mercaptoethanol, indicating that the primary substance responsible for this behavior is **hyaluronic acid**. The material revealed a non-Newtonian behavior with an irreversible disruption of the network by shear force at high speeds. The viscosity of the medium, containing about 1 microgram/ml of **hyaluronic acid**, was calculated to be similar to that of a solution containing 1.7 mg high molecular weight **hyaluronic acid** per milliliter of stock culture medium. The comparison of rheological properties between the culture medium and solutions of **hyaluronic acid** indicated the possibility of a highly organized network in the culture medium that is more complicated than a simple interaction between homologous **hyaluronic acid** molecules. The non-Newtonian behavior depends on the **hyaluronic acid**

concentration in the medium as well as on the length of exposure of the 3T3-L1 cells to the isobutyl-methylxanthine/dexamethasone mixture. The results point toward the possibility of interaction between **hyaluronic acid** and binding proteins.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Adipose Tissue: DE, drug effects
*Adipose Tissue: PH, physiology
Cell Differentiation: DE, drug effects
*Culture Media: CH, chemistry
Dexamethasone: PD, pharmacology
Gels: ME, metabolism
***Hyaluronic Acid: PD, pharmacology**
Mice
Proteoglycans: PD, pharmacology
*Rheology
Stem Cells: DE, drug effects
***Stem Cells: PH, physiology**
Viscosity
1-Methyl-3-isobutylxanthine: PD, pharmacology
3T3 Cells

RN 28822-58-4 (1-Methyl-3-isobutylxanthine); 50-02-2 (Dexamethasone); **9004-61-9 (Hyaluronic Acid)**

CN 0 (Culture Media); 0 (Gels); 0 (Proteoglycans)

L47 ANSWER 16 OF 40 MEDLINE
AN 93246642 MEDLINE
DN 93246642
TI Regulated expression of a receptor for **hyaluronan**-mediated motility on human thymocytes and T cells.
AU **Pilarski L M;** Miszta H; Turley E A
CS Department of Immunology, University of Alberta, Edmonton, Canada.
SO JOURNAL OF IMMUNOLOGY, (1993 May 15) 150 (10) 4292-302.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199308
AB A receptor for **hyaluronan**-mediated motility (RHAMM) has been shown to promote cell locomotion. Among human T lineage lymphocytes, RHAMM is expressed only on a subset of thymocytes, being absent on mature peripheral T cells from blood, spleen, and lymph node. Among thymocytes, RHAMM is selectively expressed on a subset of CD3+ CD45RA+R0+ cells, and functions in motility as shown by the ability of anti-RHAMM to reduce the speed of thymocyte locomotion from 11 microns/minute to 3 microns/min. Although freshly isolated multi-negative (MN) thymocytes (CD3-4-8-19-) lack RHAMM, its expression is induced on day 3 of culture in a variety of conditions that support differentiation, as assessed by acquisition of CD3. When MN thymocytes are cultured on plates coated with fibronectin, expression of RHAMM is prolonged, but on uncoated surfaces, its expression is transient and lost by day 7 of culture with PHA or IL-2. Culture of MN thymocytes on thymic epithelial layers, with or without IL-2, resulted in a lack of RHAMM expression. Because in the absence of epithelial cells, RHAMM is expressed, the effect appears to be one of inhibition. Although expression of RHAMM by MN thymocytes cultured with IL-2 on uncoated surfaces is transient, addition of cyclosporin A resulted in prolonged expression. These observations are consistent with the view that cyclosporin A inactivates a RHAMM-directed inhibitory mechanism. Mature peripheral blood T cells transiently express RHAMM upon culture with PHA, PMA, or IL-2. T cells that expressed RHAMM after culture with PMA alone lacked RHAMM when stimulated by mitogenic CD2 antibodies with or without CD28 antibody, indicating inhibition of RHAMM expression. Thus expression of RHAMM is regulated by a RHAMM-directed inhibitory mechanism induced by stimulation through CD2/CD28. A similar mechanism may operate in thymocyte/epithelial cell cultures. These results suggest the inhibition of RHAMM during early, presumably sessile, thymic progenitor development,

followed by its induction during developmental stages when locomotion is required. The apparently strong negative regulatory control over RHAMM expression by microenvironmental factors and by known thymic and T cell signaling molecules supports this view.

CT Check Tags: Human; Support, Non-U.S. Gov't
Antigens, CD: IM, immunology
Antigens, CD3: AN, analysis
Antigens, CD45: AN, analysis
Antigens, Differentiation, T-Lymphocyte: IM, immunology
*Carrier Proteins: ME, metabolism
Cell Differentiation
Cell Movement
Hyaluronic Acid: ME, metabolism
***Hyaluronic Acid: PD, pharmacology**
*Receptors, Cell Surface: ME, metabolism
Receptors, Immunologic: IM, immunology
Signal Transduction
T-Lymphocyte Subsets: CY, cytology
*T-Lymphocyte Subsets: ME, metabolism
*Thymus Gland: ME, metabolism

RN **9004-61-9 (Hyaluronic Acid)**

CN 0 (Antigens, CD); 0 (Antigens, CD2); 0 (Antigens, CD28); 0 (Antigens, CD3); 0 (Antigens, CD44); 0 (Antigens, CD45); 0 (Antigens, Differentiation, T-Lymphocyte); 0 (Carrier Proteins); 0 (Receptors, Cell Surface); 0 (Receptors, Immunologic)

L47 ANSWER 17 OF 40 MEDLINE

AN 93168870 MEDLINE

DN 93168870

TI [The mechanism of the steric exclusion of cells brought about by proteoglycans].
Izuchenie mekhanizma stericheskogo iskliucheniia kletok, osushchestvliaemogo proteoglikanami.

AU Bychkov S M; Kuz'mina S A

SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1992 Oct)** 114 (10) 360-2.
Journal code: A74. ISSN: 0365-9615.

CY RUSSIA: Russian Federation

DT Journal; Article; (JOURNAL ARTICLE)

LA Russian

FS Priority Journals

EM 199305

AB The effect of amount of rabbit erythrocytes and concentration of **sodium hyaluronate** and sodium salt of protein--chondroitin-keratan-sulfate were studied on aggregation of erythrocytes suspended in 0.15 M NaCL, pH 7.4. It was shown that the rate of steric exclusion of erythrocytes depends on relationship between amount of erythrocytes and concentrations of these proteoglycans.

CT Check Tags: Animal
Dose-Response Relationship, Drug
English Abstract
Erythrocyte Aggregation: DE, drug effects
Erythrocyte Count: DE, drug effects
Erythrocytes: CH, chemistry
***Erythrocytes: DE, drug effects**
Hyaluronic Acid: PD, pharmacology
Keratan Sulfate: PD, pharmacology
Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Rabbits
Solutions

RN **9004-61-9 (Hyaluronic Acid)**; 9056-36-4 (Keratan Sulfate)

CN 0 (keratan sulfate proteoglycan); 0 (Proteochondroitin Sulfates); 0 (Proteoglycans); 0 (Solutions)

L47 ANSWER 18 OF 40 MEDLINE

AN 93136433 MEDLINE
DN 93136433
TI Expression and function of a receptor for **hyaluronan**-mediated motility on normal and malignant B lymphocytes.
AU Turley E A; Belch A J; Poppema S; **Pilarski L M**
CS Manitoba Institute for Cell Biology, University of Manitoba, Canada.
NC CA51540 (NCI)
SO BLOOD, (1993 Jan 15) 81 (2) 446-53.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199304
AB Migration through extracellular matrix is fundamental to malignant invasion. A receptor for **hyaluronan**-mediated motility (RHAMM) has previously been shown to play a fundamental role in locomotion of ras-transformed cells as well as functioning in signal transduction. Expression of RHAMM was characterized on B lymphocytes from normal and malignant lymphoid tissues using multiparameter phenotypic immunofluorescence analysis as well as functional analysis of its role in locomotion of malignant hairy cell leukemia B cells. RHAMM is not detectable on most normal B cells located in blood, spleen, or lymph node, but it is detectable on bone marrow and thymic B cells. Among B-cell malignancies, it is expressed on most terminally differentiated B cells from multiple myeloma bone marrows, is present on a subset of non-Hodgkin's lymphomas, and is absent on B chronic lymphocytic leukemia. Activation of peripheral blood B cells by Staphylococcus A cowan (SAC), but not by pokeweed mitogen, induced transient expression of RHAMM at day 3 of culture, suggesting RHAMM may be used by antigen-activated normal B cells. For malignant cells, expression of RHAMM increased on long-term culture of bone marrow plasma cells from multiple myeloma patients, indicating prolonged expression in contrast to the transient expression on SAC-activated normal B cells. Intriguingly, RHAMM was expressed on hairy leukemia cells located in spleen but absent from those in peripheral blood of the same patient. RHAMM, as expressed on splenic hairy cells, was a 58-Kd molecule that binds **hyaluronan**, is encoded by a 5.2-kb messenger RNA, and participates in locomotion by these cells. Hairy cells locomoted in response to **hyaluronan** at 4 mu per minute. Monoclonal antibody to RHAMM inhibited this locomotion almost completely as detected using video time-lapse cinemicrography. These observations are consistent with a role for RHAMM in malignant invasion and metastatic growth.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
B-Lymphocytes: DE, drug effects
B-Lymphocytes: PA, pathology
*B-Lymphocytes: PH, physiology
Carrier Proteins: AN, analysis
*Carrier Proteins: ME, metabolism
*Cell Movement: DE, drug effects
Cells, Cultured
***Hyaluronic Acid: PD, pharmacology**
Leukemia, B-Cell: IM, immunology
*Leukemia, B-Cell: PP, physiopathology
Leukemia, Hairy Cell: IM, immunology
*Leukemia, Hairy Cell: PP, physiopathology
Lymphoid Tissue: IM, immunology
Lymphoid Tissue: PH, physiology
Lymphoma: IM, immunology
*Lymphoma: PP, physiopathology
Multiple Myeloma: IM, immunology
*Multiple Myeloma: PP, physiopathology
Receptors, Cell Surface: AN, analysis
*Receptors, Cell Surface: ME, metabolism
Reference Values
Tumor Cells, Cultured

RN **9004-61-9 (Hyaluronic Acid)**
CN 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Receptors, Cell Surface)

L47 ANSWER 19 OF 40 MEDLINE
AN 92019920 MEDLINE
DN 92019920
TI [The role of glycosaminoglycans in the local regulation of hemopoiesis in exposure of the body to extreme factors].
Rol' glikozaminoglikanov v lokal'noi reguliastii gemopoeza pri vozdeistvii na organizm ekstremal'nykh faktorov.
AU Iastrebov A P; Iushkov B G; Savel'ev L I
SO PATOLOGICHESKAIA FIZIOLOGIIA I EKSPERIMENTALNAIA TERAPIIA, **(1991 May-Jun)** (3) 10-2.
Journal code: OTF. ISSN: 0031-2991.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
EM 199201
AB The authors studied the role of glycosaminoglycans as component of hematopoiesis-inducing microenvironment in the regulation of hematopoiesis. Following injection of preparations of these compounds to experimental animals (male CBA mice), their concentration changed most markedly in the bone marrow and spleen. The effect of acid glycosaminoglycans on the hematopoietic cells is realized through an increase of the concentration of calcium, cAMP, and leads to activation of granulocytopoiesis. It was shown in experiments with heparin that desulfation has no effect on their hematopoietic activity.
CT Check Tags: Animal; Male
Bone Marrow: CH, chemistry
Bone Marrow: DE, drug effects
English Abstract
Glycosaminoglycans: AN, analysis
*Glycosaminoglycans: PH, physiology
***Hematopoiesis: DE, drug effects**
Hematopoiesis: PH, physiology
Heparin: AA, analogs & derivatives
Heparin: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
Mice
Mice, Inbred CBA
Spleen: CH, chemistry
Spleen: DE, drug effects
Time Factors
RN **9004-61-9 (Hyaluronic Acid)**; 9005-49-6 (Heparin)
CN 0 (heparin, N-desulfated); 0 (Glycosaminoglycans)

L47 ANSWER 20 OF 40 MEDLINE
AN 91013848 MEDLINE
DN 91013848
TI The effect of intraperitoneal administration of sodium tolmetin-**hyaluronic acid** on the postsurgical cell infiltration in vivo.
AU Abe H; Rodgers K E; Campeau J D; Girgis W; Ellefson D; DiZerega G S
CS Department of Obstetrics and Gynecology, University of Southern California, School of Medicine, Los Angeles 90033..
SO JOURNAL OF SURGICAL RESEARCH, **(1990 Oct)** 49 (4) 322-7.
Journal code: K7B. ISSN: 0022-4804.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199101
AB Intraperitoneal administration of sodium tolmetin-**hyaluronic acid** reduced the formation of adhesions at early postsurgical time points. In addition, at 6, 48, 72, and 96 hr following surgery, there was a significant reduction in the number of red blood cells (RBC) recovered

from peritoneal lavage. This effect was not the result of fluid or viscous solution in the peritoneal cavity since intraperitoneal administration of Ringer's lactate or Hyskon (a 32% solution of Dextran 70) did not affect RBC recovery. In contrast, the influx of leukocytes into the peritoneal cavity was elevated at 12 hr after surgery, but suppressed at 96 hr. These data may suggest a mechanism by which sodium tolmetin in **hyaluronic acid** reduced adhesion formation.

CT Check Tags: Animal; Female
Adhesions: ET, etiology
Adhesions: PA, pathology
*Adhesions: PC, prevention & control
Anti-Inflammatory Agents, Non-Steroidal: AD, administration & dosage
*Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use
Erythrocyte Count
Erythrocytes: PA, pathology
***Hyaluronic Acid: AD, administration & dosage**
Leukocyte Count
Macrophages: PA, pathology
Neutrophils: PA, pathology
*Peritoneal Cavity
Peritoneal Cavity: PA, pathology
Peritoneal Lavage
*Postoperative Complications
Rabbits
Time Factors
Tolmetin: AD, administration & dosage
*Tolmetin: TU, therapeutic use
Uterus: SU, surgery

RN 26171-23-3 (Tolmetin); **9004-61-9 (Hyaluronic Acid)**

L47 ANSWER 21 OF 40 MEDLINE
AN 90199921 MEDLINE
DN 90199921
TI **Hyaluronic acid** promotes chick embryo fibroblast and chondroblast expression.
AU Cortivo R; De Galateo A; Castellani I; Brun P; Giro M G; Abatangelo G
CS Institute of Histology and Embryology, University of Padua, Italy..
SO CELL BIOLOGY INTERNATIONAL REPORTS, **(1990 Feb)** 14 (2) 111-22.
Journal code: CRC. ISSN: 0309-1651.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199007
AB 15-day-chick-embryo fibroblasts and chondroblasts were cultured in the presence of high and low molecular weight exogenous **hyaluronic acid** (HA). Growth range and incorporation of radiolabelled sulphate and proline were determined. HA reduced cell proliferation to about 75% of controls, while incorporation of radiolabelled sulphate and proline was higher in HA-treated cultures of both chondroblasts and fibroblasts. The effect was not due to the polyanionic or polymeric nature of the molecule and appeared to be highly specific for HA.

CT Check Tags: Animal
Cartilage: CY, cytology
*Cartilage: DE, drug effects
Cartilage: SE, secretion
Cell Division: DE, drug effects
Cells, Cultured
Chick Embryo
Collagen
Fibroblasts: CY, cytology
***Fibroblasts: DE, drug effects**
Fibroblasts: SE, secretion
Fibronectins
***Hyaluronic Acid: PD, pharmacology**
Molecular Weight

Proline: ME, metabolism
Proteins: BI, biosynthesis
Sulfates: ME, metabolism
Tritium
RN 10028-17-8 (Tritium); 147-85-3 (Proline); **9004-61-9 (Hyaluronic Acid)**; 9007-34-5 (Collagen)
CN 0 (Fibronectins); 0 (Sulfates)

L47 ANSWER 22 OF 40 MEDLINE
AN 90034277 MEDLINE
DN 90034277
TI The effects of **hyaluronic acid** on macrophage Fc receptor binding and phagocytosis are independent of the mode of depolymerization.
AU McNeil J D; Wiebkin O W; Cleland L G; Skosey J L
CS Department of Pathology, University of Adelaide, South Australia.
SO FREE RADICAL RESEARCH COMMUNICATIONS, **(1989)** 6 (4) 227-33.
Journal code: FRR. ISSN: 8755-0199.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
AB In order to determine whether exposure of **hyaluronic acid** to oxygen radicals caused an alteration in its properties, independent of the change in molecular weight induced, we examined its effect upon macrophage Fc receptor binding. High molecular weight **hyaluronic acid** (Healon-Pharmacia) caused a dose dependent inhibition of binding between the concentrations of 0.2-1 mg/ml. At a concentration of 0.3 mg/ml both oxygen radical depolymerized and enzymatically degraded **hyaluronic acid** caused an inhibition of Fc receptor binding at molecular weights of 1 x 10(6), 1.5 x 10(6) and 2 x 10(6). Oxygen radical degraded **hyaluronic acid** caused a stimulation of Fc receptor binding at molecular weights of 2 x 10(5) and 3.5 x 10(5), and enzyme degraded **hyaluronic acid** causes stimulation at a molecular weight of 2.5 x 10(6). Thus this "biological property" of **hyaluronic acid** is dependent upon molecular weight solely and not upon the mode of depolymerization.
CT Check Tags: Human; In Vitro; Support, Non-U.S. Gov't
Azure Stains
Erythrocytes: IM, immunology
Free Radicals
Hyaluronic Acid: ME, metabolism
***Hyaluronic Acid: PD, pharmacology**
Hyaluronoglucosaminidase: ME, metabolism
*Macrophages: DE, drug effects
Macrophages: ME, metabolism
Molecular Weight
Monocytes: DE, drug effects
*Phagocytosis: DE, drug effects
*Receptors, Fc: DE, drug effects
Receptors, Fc: ME, metabolism
RN **9004-61-9 (Hyaluronic Acid)**
CN EC 3.2.1.35 (Hyaluronoglucosaminidase); 0 (Azure Stains); 0 (Free Radicals); 0 (Receptors, Fc)

L47 ANSWER 23 OF 40 MEDLINE
AN 89380548 MEDLINE
DN 89380548
TI Glycosaminoglycans facilitate the movement of fibroblasts through three-dimensional collagen matrices.
AU Docherty R; Forrester J V; Lackie J M; Gregory D W
CS Department of Cell Biology, University of Glasgow..
SO JOURNAL OF CELL SCIENCE, **(1989 Feb)** 92 (Pt 2) 263-70.
Journal code: HNK. ISSN: 0021-9533.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198912
AB The effect of glycosaminoglycans on the invasion of choroid fibroblasts into type I collagen gels was studied. Both **hyaluronate** and chondroitin sulphate, when incorporated into the gel, facilitated invasion of the collagen matrix, although **hyaluronate** was considerably more effective. **Hyaluronate**-induced fibroblast invasion was markedly concentration-dependent, being reduced at both high and low concentrations. Increased cell invasion appeared to correlate with denser packing of collagen fibrils within the gel, since the same effect could be achieved by increasing the collagen concentration of native, i.e. glycosaminoglycan-free gels. Scanning electron microscopy of the interior of the collagen gels suggested that changes in packing arrangement of fibrils in gels that had polymerized in the presence of glycosaminoglycans might account in part for different rates of cell invasion.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Movement
Chick Embryo
Chondroitin Sulfates: PD, pharmacology
Choroid: CY, cytology
*Collagen
***Fibroblasts: PH, physiology**
Fibroblasts: UL, ultrastructure
Gels
*Glycosaminoglycans: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
Microscopy, Electron, Scanning
RN **9004-61-9 (Hyaluronic Acid)**; 9007-28-7 (Chondroitin Sulfates); 9007-34-5 (Collagen)
CN 0 (Gels); 0 (Glycosaminoglycans)

L47 ANSWER 24 OF 40 MEDLINE
AN 89358966 MEDLINE
DN 89358966
TI Mechanism of action of the migration stimulating factor produced by fetal and cancer patient fibroblasts: effect on hyaluronic and synthesis.
AU Schor S L; Schor A M; Grey A M; Chen J; Rushton G; Grant M E; Ellis I
CS Department of Cell and Structural Biology, University of Manchester.
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY, **(1989 Aug)** 25 (8) 737-46.
Journal code: HEQ. ISSN: 0883-8364.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198912
AB We have previously demonstrated that confluent fetal fibroblasts migrate into three-dimensional collagen gels to a significantly greater extent than their normal adult counterparts. Recent studies have revealed that this behavioral difference results from the secretion by fetal fibroblasts of a soluble migration-stimulating factor (MSF) which acts on these cells in an autocrine fashion. Adult fibroblasts do not produce MSF but remain responsive to it. Skin fibroblasts from cancer patients resemble fetal fibroblasts (rather than normal adult cells) with respect to their migratory behavior on collagen gels and continued production of MSF. This communication is concerned with elucidating the biochemical basis of MSF activity. Data are presented indicating that a) **hyaluronic acid** is required for the elevated migratory activity displayed by confluent fetal and breast cancer patient skin fibroblast; b) adult fibroblasts exhibit a bell-shaped dose-response to MSF, with maximal stimulation of migration observed at a concentration of 10 ng/ml; c) the migratory activity of adult fibroblasts pre-incubated with MSF remains high in the absence of additional factor: and d) MSF affects both the

quantity and size class distribution of **hyaluronic acid** synthesized by adult fibroblasts. We have previously speculated that the persistent fetal-like fibroblasts of breast cancer patients play a direct role in disease pathogenesis by perturbing normal epithelial-mesenchymal interactions. The observations reported here suggest that MSF-induced alterations in **hyaluronic acid** synthesis may contribute to the molecular basis of such perturbations.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Cell Line
Cell Movement: DE, drug effects
Child
Chondroitinases and Chondroitin Lyases: PD, pharmacology
Culture Media: PD, pharmacology
Cytokines: ME, metabolism
Epithelium: ME, metabolism
Epithelium: PA, pathology
Fetus: CY, cytology
Fetus: ME, metabolism
Fetus: PA, pathology
***Fibroblasts: ME, metabolism**
Fibroblasts: PA, pathology
Glycosaminoglycans: ME, metabolism
***Hyaluronic Acid: ME, metabolism**
Hyaluronic Acid: PD, pharmacology
Hyaluronoglucosaminidase: PD, pharmacology
*Lymphokines: ME, metabolism
Lymphokines: PD, pharmacology
Lymphokines: PH, physiology
Mesoderm: ME, metabolism
Mesoderm: PA, pathology
Middle Age
Polysaccharide-Lyases: PD, pharmacology

RN **9004-61-9 (Hyaluronic Acid)**

CN EC 3.2.1.35 (Hyaluronoglucosaminidase); EC 4.2.2. (Polysaccharide-Lyases); EC 4.2.2.- (Chondroitinases and Chondroitin Lyases); EC 4.2.2.7 (Heparin Lyase); 0 (migration stimulating factor); 0 (Culture Media); 0 (Cytokines); 0 (Glycosaminoglycans); 0 (Lymphokines)

L47 ANSWER 25 OF 40 MEDLINE

AN 89234253 MEDLINE

DN 89234253

TI **Hyaluronic acid** modulates proliferation of mouse dermal fibroblasts in culture.

AU Yoneda M; Yamagata M; Suzuki S; Kimata K

CS Department of Chemistry, Faculty of Science, Nagoya University, Japan..

SO JOURNAL OF CELL SCIENCE, **(1988 Jun)** 90 (Pt 2) 265-73.
Journal code: HNK. ISSN: 0021-9533.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198908

AB When the concentration of **hyaluronic acid** was monitored in primary cultures of mouse skin dermal fibroblasts, there was an increase in **hyaluronic acid** proportional to the increase in cell number during the logarithmic growth phase. The concentration reached the maximum value 2 days before the cells became confluent, and then decreased gradually. **Hyaluronic acid** added at 1 mg ml-1 during the logarithmic phase either promoted or inhibited cell growth, depending on the density of cells at the time when **hyaluronic acid** was added. **Hyaluronic acid** (1 mg ml-1) added to subconfluent or postconfluent cultures induced a transient DNA synthesis with a consequent increase (greater than 20%) in cell number. The effects appeared to be specific, since neither **hyaluronic acid** oligosaccharides nor some other types of glycosaminoglycan (chondroitin, chondroitin sulphates, heparan sulphates

and heparin) had any similar effects. Dibutyryl adenosine 3',5'-cyclic monophosphate (dbcAMP), at 1 mM, added to subconfluent or postconfluent cultures had promoting effects successively on **hyaluronic acid** synthesis and on cell growth. An increase in **hyaluronic acid** synthesis also occurred when dbcAMP was added to day 1 cultures in the logarithmic growth phase, but the effect on cell growth was reversed; there was an inhibition rather than a promotion. The pattern of cell density-dependent variation of the dbcAMP effect is quite similar to that observed with exogenously added **hyaluronic acid**. Therefore, we propose that **hyaluronic acid** added exogenously or supplied endogenously by increased synthesis may act as a modulator of mouse dermal fibroblast proliferation.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Bucladesine: PD, pharmacology
Cell Division: DE, drug effects
Cells, Cultured
DNA: BI, biosynthesis
***Fibroblasts: DE, drug effects**
Fibroblasts: ME, metabolism
Hyaluronic Acid: BI, biosynthesis
***Hyaluronic Acid: PD, pharmacology**
Mice
Mice, Inbred Strains
*Skin: DE, drug effects

RN 362-74-3 (Bucladesine); **9004-61-9 (Hyaluronic Acid)**; 9007-49-2 (DNA)

L47 ANSWER 26 OF 40 MEDLINE
AN 89062679 MEDLINE
DN 89062679
TI [The role of different proteoglycan salts as factors in steric exclusion]. Rol' razlichnykh solei proteoglikanov kak faktorov stericheskogo iskliucheniia.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1988 Nov)** 106 (11) 545-7.
Journal code: A74. ISSN: 0365-9615.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals; Cancer Journals
EM 198903
AB It has been shown that the capacity of Ca2+ salts of **hyaluronic acid** (HA) and nonaggregating protein-chondroitin-keratan-sulfate (PCKS) to divide in erythrocyte-saline suspension into liquid and cell phases was stronger than the analogous capacity of K+ salts. It was suggested that this is connected with a tendency to form different three-dimensional structures in solutions, which was more expressed in HA and PCKS Ca2+ salts than in K+ salts of these proteoglycans.

CT Check Tags: Animal; Comparative Study
Calcium: PD, pharmacology
Dose-Response Relationship, Drug
English Abstract
Erythrocytes: DE, drug effects
Hyaluronic Acid: PD, pharmacology
Keratan Sulfate: PD, pharmacology
Molecular Conformation
Potassium: PD, pharmacology
Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Rabbits
Solutions
Suspensions

RN 7440-09-7 (Potassium); 7440-70-2 (Calcium); **9004-61-9 (Hyaluronic Acid)**; 9056-36-4 (Keratan Sulfate)
CN 0 (keratan sulfate proteoglycan); 0 (Proteochondroitin Sulfates); 0

(Proteoglycans); 0 (Solutions); 0 (Suspensions)

L47 ANSWER 27 OF 40 MEDLINE
AN 88290610 MEDLINE
DN 88290610
TI Fibroblast and epidermal cell-type I collagen interactions: cell culture and human studies.
AU Doillon C J; Silver F H; Olson R M; Kamath C Y; Berg R A
CS Department of Pathology, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Piscataway 08854..
SO SCANNING MICROSCOPY, **(1988 Jun)** 2 (2) 985-92.
Journal code: UEC. ISSN: 0891-7035.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198811
AB Fibroblast and epidermal cell-type I collagen sponge interactions were studied in cell culture as well as in humans. In cell culture, fibroblasts were observed to migrate and proliferate throughout a type I collagen sponge containing either **hyaluronic acid** (HA) or fibronectin (FN). Fibroblasts accumulated in the center of the pores in sponges containing HA and appeared to surround themselves with newly synthesized extracellular matrix. In sponges containing FN, fibroblasts attached to and elongated along the collagen fibers of the sponge. In the absence of FN or HA protein synthesis of fibroblasts appeared to be inhibited by the presence of the type I collagen sponge. Epidermal cells grown on plastic or on type I collagen, formed sheets. Epidermal cells grown on a collagen sponge morphologically appeared different than cells grown on plastic. The type I collagen matrix studied in cell culture was applied to dermal wounds of patients with pressure ulcers in order to evaluate its effect on dermal wound healing. The areas of ulcers treated for 6 weeks with a type I collagen sponge decreased by about 40% compared with no change in the areas of untreated controls. Preliminary results suggest that a type I collagen sponge is a biocompatible substrate with fibroblasts and epidermal cells and may be effective in enhancing healing of chronic skin ulcers.
CT Check Tags: Animal; Human
Cattle
Cells, Cultured
*Collagen: TU, therapeutic use
*Decubitus Ulcer: TH, therapy
***Fibroblasts: CY, cytology**
Fibronectins: TU, therapeutic use
Hyaluronic Acid: TU, therapeutic use
*Skin: CY, cytology
Skin: PA, pathology
*Wound Healing
RN **9004-61-9 (Hyaluronic Acid)**; 9007-34-5 (Collagen)
CN 0 (Fibronectins)

L47 ANSWER 28 OF 40 MEDLINE
AN 88163885 MEDLINE
DN 88163885
TI Behaviour of fibroblasts and epidermal cells cultivated on analogues of extracellular matrix.
AU Doillon C J; Wasserman A J; Berg R A; Silver F H
CS Department of Pathology, UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ 08854..
SO BIOMATERIALS, **(1988 Jan)** 9 (1) 91-6.
Journal code: A4P. ISSN: 0142-9612.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198807

AB A porous collagen sponge can be used for supporting epidermal cells and fibroblasts in order to manufacture an artificial skin. Fibroblasts were grown on analogues of extracellular matrix containing collagen and glycosaminoglycans and/or glycoproteins. Cell replication, and also infiltration of fibroblasts, were enhanced by the presence of **hyaluronic acid** and/or fibronectin. Epidermal cells grown on a collagen sponge have been characterized by microscopic observations. Epidermal cells on the surface of the sponge showed an incomplete differentiation in comparison to normal skin; clumps of epidermal cells were found in the interior of the sponge. Epidermal cell replication was enhanced in the presence of collagen sponge seeded with fibroblasts.

CT Check Tags: Animal; Support, Non-U.S. Gov't
*Biocompatible Materials
Cell Differentiation
Cell Division
Cells, Cultured
Chick Embryo
Collagen
*Epidermis: CY, cytology
Epidermis: DE, drug effects
*Extracellular Matrix
***Fibroblasts: CY, cytology**
Fibroblasts: DE, drug effects
Fibronectins: PD, pharmacology
Glycoproteins
Glycosaminoglycans
Guinea Pigs
Hyaluronic Acid: PD, pharmacology
Microscopy, Electron

RN **9004-61-9 (Hyaluronic Acid)**; 9007-34-5 (Collagen)

CN 0 (Biocompatible Materials); 0 (Fibronectins); 0 (Glycoproteins); 0 (Glycosaminoglycans)

L47 ANSWER 29 OF 40 MEDLINE

AN 88143546 MEDLINE

DN 88143546

TI Implantation of fibroblasts into vitrectomized eyes. Dose-response relationship and the putative inhibitory effect of **sodium hyaluronate.**

AU Algvere P; Landau I M

CS Department of Ophthalmology, Karolinska Institute and Hospital, Stockholm, Sweden..

SO OPHTHALMIC RESEARCH, **(1987)** 19 (5) 271-6.
Journal code: OIE. ISSN: 0030-3747.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198806

AB To determine whether or not **sodium hyaluronate** (NaHA) has any inhibitory effect on cellular proliferation in the vitreous space, we implanted 3 X 10(5) or 1 X 10(6) homologous fibroblasts into the vitreous cavity of 21 vitrectomized albino rabbits. Sixteen eyes received 0.7-0.8 ml of a 1% solution of NaHA intravitreally and 18 eyes got BSS only. Ophthalmoscopy and histological examination showed that 5 of 10 BSS-injected and 2 of 8 NaHA-injected eyes in the group receiving 3 X 10(5) fibroblasts developed retinal detachment (RD) after 4-8 weeks. All BSS- and NaHA-injected eyes implanted with 1 X 10(6) fibroblasts developed RD. The results indicate that NaHA has an unsatisfactory inhibitory effect on fibrovascular growth in response to moderate and large inocula of fibroblasts.

CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Cell Division: DE, drug effects
Dose-Response Relationship, Drug
Fibroblasts: PA, pathology

***Fibroblasts: TR, transplantation**
***Hyaluronic Acid: PD, pharmacology**
Injections
Rabbits
Retinal Detachment: ET, etiology
Skin
Sodium Chloride: PD, pharmacology
*Vitrectomy
*Vitreous Body: PA, pathology
RN 7647-14-5 (Sodium Chloride); **9004-61-9 (Hyaluronic Acid)**

L47 ANSWER 30 OF 40 MEDLINE
AN 87101407 MEDLINE
DN 87101407
TI [Role of heparin in erythrocyte aggregation].
Rol' geparina v agregatsii eritrotsitov.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1986 Dec)** 102 (12) 692-5.
Journal code: A74. ISSN: 0365-9615.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals; Cancer Journals
EM 198705
AB The effect of two heparin fractions containing 3 (HP-3) and 4 (HP-4) residues of sulfuric acid per dimer of polymers on the capacity of **hyaluronate** potassium (HUP) and protein-chondroitin-keratan-sulfate potassium (PCHKSP) to aggregate rabbit erythrocytes suspended in 0.15 M NaCl was studied. HP-3 (0.3-5.0 mg X ml-1) and HP-4 (0.3-5.0 mg X ml-1) was inhibited the aggregating action on the erythrocytes of HUP. Fraction HP-3 (0.3-5.0 mg X ml-1) was activated the aggregating action on the erythrocytes of PCHKSP. Fraction HP-4 when the concentration of their biopolymer were 0.3 mg X ml-1 so activated the aggregating action of PCHKSP, but when the concentration HP-4 0.6-5.0 mg X ml-1 was inhibited the aggregating action PCHKSP. The mixture of HP-3 (1.2 mg X ml-1) and HP-4 (1.2 mg X ml-1) was not influenced on aggregating action of PCHKSP.
CT Check Tags: Animal; In Vitro
Dose-Response Relationship, Drug
Drug Interactions
English Abstract
***Erythrocyte Aggregation: DE, drug effects**
*Heparin: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
Keratan Sulfate: PD, pharmacology
Proteochondroitin Sulfates: PD, pharmacology
Rabbits
Solutions
RN **9004-61-9 (Hyaluronic Acid)**; 9005-49-6 (Heparin); 9056-36-4 (Keratan Sulfate)
CN 0 (keratan sulfate proteoglycan); 0 (Proteochondroitin Sulfates); 0 (Solutions)

L47 ANSWER 31 OF 40 MEDLINE
AN 87091010 MEDLINE
DN 87091010
TI Delivery of antifibroblast agents as adjuncts to filtration surgery. Part I--Periocular clearance of cobalt-57 bleomycin in experimental drug delivery: pilot study in the rabbit.
AU Kay J S; Litin B S; Woolfenden J M; Chvapil M; Herschler J
NC EY03655 (NEI)
SO OPHTHALMIC SURGERY, **(1986 Oct)** 17 (10) 626-30.
Journal code: OIC. ISSN: 0022-023X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 198704
AB Antitumor and antifibroblast agents show promise as adjuncts after glaucoma filtration surgery in reducing postoperative scarring and failure. We used nuclear imaging in rabbits to investigate periocular clearance of one such agent (57Co-bleomycin). Sub-Tenon injection was compared to other delivery techniques. Our results showed that a collagen sponge and a silastic disc implant with a microhole prolonged drug delivery when compared to sub-Tenon injection alone or injection with a viscosity enhancing agent (0.5% **sodium hyaluronate**).
We theorize that if an antifibroblast agent can be delivered in small and sustained amounts after filtration surgery, this may prolong bleb longevity and avoid unnecessary drug toxicity.
CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Bleomycin: AD, administration & dosage
*Bleomycin: ME, metabolism
Cell Division: DE, drug effects
*Cobalt Radioisotopes: DU, diagnostic use
Collagen
Drug Implants
Eye: ME, metabolism
*Eye: SU, surgery
***Fibroblasts: DE, drug effects**
Filtration
Hyaluronic Acid: AD, administration & dosage
Injections
Pilot Projects
Postoperative Care
Rabbits
Silicone Elastomers
Time Factors
RN 11056-06-7 (Bleomycin); **9004-61-9 (Hyaluronic Acid)**; 9007-34-5 (Collagen)
CN 0 (Cobalt Radioisotopes); 0 (Drug Implants); 0 (Silicone Elastomers)

L47 ANSWER 32 OF 40 MEDLINE
AN 85047476 MEDLINE
DN 85047476
TI [2 functions of proteoglycans in erythrocyte aggregation and adhesion]. O dvukh funtsiiakh proteoglikanov v agregatsii i adgezii eritrotsitov.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1984 Oct)** 98 (10) 410-3.
Journal code: A74. ISSN: 0365-9615.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals; Cancer Journals
EM 198503
AB It has been shown that rabbit red cells treated with formalin form aggregates in the presence of **hyaluronic acid** (HUA) soluble protein-chondroitin-keratan sulfate (PCKS) and cartilage proteoglycan aggregates (PA) but to a lesser degree than normal red cells. It is suggested that the proteoglycans under consideration can specifically interact with red cells. Aggregation of red cells in the presence of HUA, PCKS and PA is the result of the combined action of these two factors.
CT Check Tags: Animal
Cell Adhesion: DE, drug effects
English Abstract
***Erythrocyte Aggregation: DE, drug effects**
***Erythrocytes: DE, drug effects**
Formaldehyde: PD, pharmacology
Hyaluronic Acid: PD, pharmacology
Keratan Sulfate: PD, pharmacology

Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Rabbits
Suspensions
RN 50-00-0 (Formaldehyde); **9004-61-9 (Hyaluronic Acid)**; 9056-36-4 (Keratan Sulfate)
CN 0 (keratan sulfate proteoglycan); 0 (Proteochondroitin Sulfates); 0 (Proteoglycans); 0 (Suspensions)

L47 ANSWER 33 OF 40 MEDLINE
AN 79068786 MEDLINE
DN 79068786
TI Stimulatory effect of exogenous **hyaluronic acid** distinguishes cultured fibroblasts of Marfan's disease from controls.
AU Lamberg S I
SO JOURNAL OF INVESTIGATIVE DERMATOLOGY, **(1978 Dec)** 71 (6) 391-5.
Journal code: IHZ. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197904
AB Fibroblasts cultured from patients with Marfan's disease show metachromasia with toluidine blue and accumulate increased amounts of glycosaminoglycan (GAG). Compared to fibroblasts from controls, more of the newly synthesized GAG is **hyaluronic acid**.
Cycloheximide has a modest inhibiting effect on GAG accumulation compared to protein inhibition while serum depletion has a greater effect on inhibiting GAG accumulation than on reducing synthesis of new protein.
Exogenous **hyaluronic acid** restores new accumulation of **hyaluronic acid** in serum depleted Marfan-derived cultures towards baseline while having almost no effect on cultures derived from controls. The effect is specific for **hyaluronic acid** as chondroitin sulfate or dextran sulfate are not stimulatory and is not due to stimulation of new protein synthesis.
CT Check Tags: Comparative Study; Female; Human; In Vitro; Male
Adolescence
Adult
Cycloheximide: PD, pharmacology
***Fibroblasts: DE, drug effects**
Fibroblasts: ME, metabolism
*Glycosaminoglycans: ME, metabolism
***Hyaluronic Acid: PD, pharmacology**
*Marfan Syndrome: ME, metabolism
Marfan Syndrome: PA, pathology
Proteins: BI, biosynthesis
Skin: ME, metabolism
Skin: PA, pathology

L47 ANSWER 34 OF 40 MEDLINE
AN 78061189 MEDLINE
DN 78061189
TI [Joint action of protein-chondroitin-4-keratan-sulfate and **hyaluronic acid** on erythrocyte aggregation and adhesion].
Sovmestnoe deistvie protein-khondroitin-4-keratan-sul'fata i gialuronovoi kisloty na agregatsiiu i adgeziiu eritrotsitov.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1977 Nov)** 84 (11) 562-5.
Journal code: A74. ISSN: 0006-4041.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 197804

AB It was shown that the rate and the degree of erythrocytes aggregation brought about by a mixture of protein-chondroitin-4-keratan sulfate (PCKS) and **hyaluronic acid** (HA) was greater than the sum of the values of the corresponding indices observed during separate independent action of these proteoglycans on the aggregation of the mentioned cells concentrations as in the mixtures. It may be supposed that such phenomenon is connected with formation in the mixture of a hybrid PCKS-HA complex which is more active in respect to the erythrocyte aggregation than its components separately.

CT Cell Adhesion: DE, drug effects
Drug Synergism
English Abstract
Erythrocyte Aggregation: DE, drug effects
***Erythrocytes: DE, drug effects**
*Glycosaminoglycans: PD, pharmacology
***Hyaluronic Acid: PD, pharmacology**
*Keratan Sulfate: PD, pharmacology
*Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Stimulation, Chemical

L47 ANSWER 35 OF 40 MEDLINE
AN 77158705 MEDLINE
DN 77158705
TI [Role of glycosaminoglycans and proteoglycans in erythrocyte aggregation and adhesion].
Rol' glikozaminoglikanov i proteoglikanov v agregatsii i adgezii eritrotsitov.
AU Bychkov S M; Kuz'mina S A
SO BIULLETEN EKSPERIMENTALNOI BIOLOGII I MEDITSINY, **(1977 Mar)** 83 (3) 284-8.
Journal code: A74. ISSN: 0006-4041.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 197708
AB The action of **hyaluronate** potassium (HUK) and of protein chondroitin-4-sulphate potassium (PCHSK) on the aggregation and adhesion of rabbit erythrocytes suspended in physiological saline was studied. It was found that the capacity of HUK and PCHSK to produce an unspecific and reversible aggregation of erythrocytes was connected with the formation by these biopolymeres (in solutions) of complex structures of osmotic cell type and molecular sieves, displacing cells from the space occupied by them and concentrating them in a maximally limited volume. Different heparin fractions producing no such structures in solutions did not induce formation of such individual clear-cut erythrocyte-aggregations, but inhibited the aggregating action of HUK and PCHSK when the concentration of these biopolymeres were inadequate for the complete erythrocyte aggregation. Probably, the aggregating action of HUK and PCHSK necessary for adhesion served as one of the universal biological functions expressed not only towards the erythrocytes, but also towards the other cells and different tissue structural elements.
CT Check Tags: Animal; Comparative Study
Dose-Response Relationship, Drug
English Abstract
***Erythrocyte Aggregation: DE, drug effects**
*Heparin: PD, pharmacology
***Hyaluronic Acid: PD, pharmacology**
Kinetics
*Proteochondroitin Sulfates: PD, pharmacology
*Proteoglycans: PD, pharmacology
Rabbits

L47 ANSWER 36 OF 40 MEDLINE
AN 69107276 MEDLINE

DN 69107276
TI [Effect, on "mast cell" genesis, of constituents of mucopolysaccharides in the dermal interstice. (Preliminary note)].
Influenza sulla genesi delle "mastzellen" da parte di costituenti dei mucopolisaccaridi nell'interstizio dermico. (Nota preventiva).
AU Lo Brutto M E; Curri S B; Ziliotto G R
SO RIVISTA DI PATOLOGIA CLINICA E SPERIMENTALE, **(1967 Oct-Dec)** 8 (4) 449-61.
Journal code: TRL. ISSN: 0035-6409.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA Italian
EM 196905
CT Check Tags: Animal
*Disaccharides: PD, pharmacology
*Glycosaminoglycans: PD, pharmacology
*Granulation Tissue: CY, cytology
***Hyaluronic Acid: PD, pharmacology**
***Mast Cells**
Rats
*Skin: CY, cytology
***Wound Healing**

L47 ANSWER 37 OF 40 MEDLINE
AN 64071840 MEDLINE
DN 64071840
TI [THE **EXPLOSION** OF **HEMOGLOBIN** AND SPLITTING OF THE **ERYTHROCYTE** MEMBRANE BY **HYALURONIC ACID** AND TANNIN].
SPRENGUNG DES HAEMOGLOBINS AND SPALTUNG DER **ERYTHROCYTEN**-MEMBRAN DURCH HYALURONSAEURE UND TANNIN.
AU TOMCSIK J; LITSCHEL E
SO PATHOLOGIA ET MICROBIOLOGIA, (1963) 26 645-54.
Journal code: OST. ISSN: 0031-2959.
CY Switzerland
LA German
FS **OLDMEDLINE**
EM 196406
ST **erythrocytes**; hemoglobin; **hyaluronic acid**; pharmacology; tannins
RN 1401-55-4 (TANNINS); **9004-61-9 (HYALURONIC ACID)**

L47 ANSWER 38 OF 40 MEDLINE
AN 64059199 MEDLINE
DN 64059199
TI [PARTIAL **EXPLOSION** OF **ERYTHROCYTES**].
PARTIELLE SPRENGUNG DER **ERYTHROCYTEN**.
AU LITSCHEL E; TOMCSIK J
SO EXPERIENTIA, (1963 NOV 15) 19 583-5.
Journal code: EQZ. ISSN: 0014-4754.
CY Switzerland
LA German
FS **OLDMEDLINE**
EM 196405
ST experimental lab study; hemoglobin; hemolysis; **hyaluronic acid**; pharmacology
RN **9004-61-9 (HYALURONIC ACID)**

L47 ANSWER 39 OF 40 MEDLINE
AN 64058849 MEDLINE
DN 64058849
TI PARTIAL **EXPLOSION** OF **ERYTHROCYTES**, INDUCED BY **HYALURONIC ACID**.
AU TOMCSIK J; LITSCHEL E
SO PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE, (1963 NOV) 114 286-9.

Journal code: PXZ. ISSN: 0037-9727.
CY United States
LA English
FS **OLDMEDLINE**
EM 196405
ST **erythrocytes**; experimental lab study; hemoglobin; hemolysis; **hyaluronic acid**; hyaluronidase; hydrogen-ion concentration; pharmacology
RN **9004-61-9 (HYALURONIC ACID)**; 12408-02-5 (HYDROGEN ION); 9001-54-1Q, 37259-53-3Q, 37288-34-9Q, 37326-33-3Q (HYALURONIDASE)

L47 ANSWER 40 OF 40 MEDLINE
AN 60184181 MEDLINE
DN 60184181
TI Changes in the **blood picture** and the blood **hexosamines** following the prolonged administration of **hyaluronic acid**.
AU PELLEGRINI G; SALA M
SO Boll Soc Ital Biol Sper, (1959 Dec 31) 35 1847-51.
LA Italian
FS **OLDMEDLINE**
EM 196012
ST amino sugars - blood; blood proteins - pharmacology; **hyaluronic acid** - pharmacology
RN **9004-61-9 (HYALURONIC ACID)**

=> e stem cells+all/ct

E1	0	BT2	A Anatomy/CT
E2	4493	BT1	Cells/CT
E3	7530	-->	Stem Cells/CT
E4	82753	MN	A11.872./CT
		DC	an INDEX MEDICUS major descriptor
		NOTE	Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost.
		INDX	A 11 qualif
		AQ	CH CL CY DE EN IM ME MI PA PH PS RA RE RI SE TR UL US VI
		PNTE	Cell Differentiation (66-83)
		PNTE	Cell Line (69-83)
		PNTE	Cells, Cultured (72-83)
		PNTE	Colony-Forming Units Assay (79-83)
		HNTE	84
		MHTH	BIOETHICS 1999
		MHTH	NLM 1984
E5	0	UF	Cell, Mother/CT
E6	0	UF	Cell, Progenitor/CT
E7	0	UF	Cell, Stem/CT
E8	0	UF	Cells, Mother/CT
E9	0	UF	Cells, Progenitor/CT
E10	0	UF	Cells, Stem/CT
E11	0	UF	Colony Forming Unit/CT
E12	0	UF	Colony Forming Units/CT
E13	0	UF	Colony-Forming Unit/CT
E14	0	UF	Colony-Forming Units/CT
E15	0	UF	Mother Cell/CT
E16	0	UF	Mother Cells/CT
E17	0	UF	Progenitor Cell/CT
E18	0	UF	Progenitor Cells/CT
E19	0	UF	Stem Cell/CT
E20	0	UF	Unit, Colony-Forming/CT
E21	0	UF	Units, Colony-Forming/CT
E22	51757	NT1	Fibroblasts/CT

```
E23      11145       NT2   3T3 Cells/CT
E24       6529       NT2   L Cells (Cell Line)/CT
E25      21110      NT1   Hematopoietic Stem Cells/CT
E26       1534       NT2   Erythroid Progenitor Cells/CT
E27       1778        NT3   Erythroblasts/CT
E28       2826      NT1   Tumor Stem Cells/CT
*********  END***

=> d his l48-

     (FILE 'REGISTRY' ENTERED AT 07:33:19 ON 08 APR 2000)

     FILE 'MEDLINE' ENTERED AT 07:33:48 ON 08 APR 2000
               E STEM CELLS+ALL/CT
               E STEM CELLS+ALL/CT
L48          65 S L41 NOT L43-L47
L49         138 S L39 NOT L41,L43-L48
L50           5 S L49 AND (MEGAKARYOCYTOPOI? OR HEMATOPOIETIC SUPPORTIVE CELLS
L51           4 S L50 NOT CHICK/TI

=> d all tot

L51  ANSWER 1 OF 4  MEDLINE
AN   96257839     MEDLINE
DN   96257839
TI   Glycosaminoglycans enhance megakaryocytopoiesis by modifying the
     activities of hematopoietic growth regulators.
AU   Han Z C; Bellucci S; Shen Z X; Maffrand J P; Pascal M; Petitou M; Lormeau
     J; Caen J P
CS   Institut des Vaisseaux et du Sang, Hopital Lariboisi`ere, Paris, France.
SO   JOURNAL OF CELLULAR PHYSIOLOGY, (1996 Jul) 168 (1) 97-104.
     Journal code: HNB. ISSN: 0021-9541.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; Cancer Journals
EM   199609
AB   We have previously reported that heparin is capable of stimulating in
     vitro and in vivo megakaryocytopoiesis in mice and has a thrombopoietic
     effect when given in chronic immune thrombocytopenic purpura and that
     heparin and several other glycosaminoglycans (GAGs) promote the growth of
     human megakaryoblastic cell lines in the presence of serum. We show here
     that GAGs, including heparan sulfate (HS), chondroitin sulfate (CS),
     dermatan sulfate (DS), and hyaluronic acid (HA), also
     stimulate in vitro growth of murine megakaryocyte progenitors and augment
     the diameter of individual megakaryocytes in the presence of serum.
     However, in a serum-free agar system, the GAGs alone had no effect on
     megakaryocyte colony formation, suggesting that GAGs cooperate with some
     serum factor(s) to exert their activity. We also show that heparin
     significantly potentiates the megakaryocytopoietic activity of C-Mpl
     ligand and interleukin (IL)-6 but not IL3, GM-CSF, SCF, and Epo. In
     addition, the GAGs significantly neutralize the inhibitory action of
     platelet factor 4 (PF4) and transforming growth factor beta 1 (TGF beta 1)
     on megakaryocyte colony growth. These results demonstrate a stimulating
     activity of GAGs on megakaryocytopoiesis by modifying the activity of
     several growth-regulating factors.
CT   Check Tags: Animal; Male; Support, Non-U.S. Gov't
      Cells, Cultured
      *Glycosaminoglycans: PH, physiology
      *Growth Substances: PH, physiology
      *Hematopoiesis
       Interleukin-6: PH, physiology
      *Megakaryocytes: CY, cytology
       Mice
       Mice, Inbred BALB C
       Platelet Factor 4: PH, physiology
```

Thrombopoietin: PH, physiology
Transforming Growth Factor beta: PH, physiology
RN 37270-94-3 (Platelet Factor 4); 9014-42-0 (Thrombopoietin)
CN 0 (Glycosaminoglycans); 0 (Growth Substances); 0 (Interleukin-6); 0 (Transforming Growth Factor beta)

L51 ANSWER 2 OF 4 MEDLINE
AN 94244727 MEDLINE
DN 94244727
TI Effects of anti-CD44 monoclonal antibody on adhesion of erythroid leukemic cells (ELM-I-1) to **hematopoietic supportive cells** (MS-5): CD44, but not **hyaluronate**-mediated, cell-cell adhesion.
AU Sugimoto K; Tsurumaki Y; Hoshi H; Kadowaki S; LeBousse-Kerdiles M C; Smadja-Joffe F; Mori K J
CS Department of Physiology and Biochemistry, Faculty of Science, Niigata University, Japan..
SO EXPERIMENTAL HEMATOLOGY, **(1994 Jun)** 22 (6) 488-94.
Journal code: EPR. ISSN: 0301-472X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199408
AB Cocultivation of erythroid leukemic cells (ELM-I-1) with hemopoietic supportive cells (MS-5) resulted in a specific adhesion of ELM-I-1 cells to MS-5 cells. This phenomenon was designated as rosette formation. After induction of differentiation of ELM-I-1 cells, rosette formation was reduced, and no rosette formation was observed between erythrocytes and MS-5 cells. Studies on anti-adhesion molecule antibody treatment have revealed that CD44 plays a key role in rosette formation. Expression of CD44 on (the membrane of) ELM-I-1 cells was reduced after differentiation, and no CD44 expression was detected on erythrocytes. CD44 was also expressed on MS-5. **Hyaluronate** is known as the ligand of CD44, but neither hyaluronidase treatment nor addition of excess **hyaluronate** to the assay system affected rosette formation. These data indicate that **hyaluronate** is not responsible for rosette formation. Anti-CD44 antibody (KM81), which recognized the **hyaluronate** binding site of CD44, inhibited rosette formation. But other monoclonal antibodies against different epitopes except for the **hyaluronate** binding site, even those against CD44's **hyaluronate** binding site, did not inhibit rosette formation. Thus, rosette formation between MS-5 cells and ELM-I-1 cells is mediated by CD44 but not by the **hyaluronate** binding site of CD44.
CT Check Tags: Animal; Human; In Vitro; Support, Non-U.S. Gov't
Antibodies, Monoclonal: IM, immunology
*Carrier Proteins: PH, physiology
Cell Adhesion
Cell Line
***Hematopoiesis**
Hyaluronic Acid: PH, physiology
*Leukemia, Erythroblastic, Acute: PA, pathology
Ligands
Mice
*Receptors, Cell Surface: PH, physiology
*Receptors, Lymphocyte Homing: PH, physiology
Rosette Formation
RN **9004-61-9 (Hyaluronic Acid)**
CN 0 (Antibodies, Monoclonal); 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Ligands); 0 (Receptors, Cell Surface); 0 (Receptors, Lymphocyte Homing)

L51 ANSWER 3 OF 4 MEDLINE
AN 81147191 MEDLINE
DN 81147191
TI Effect of short- or long-term treatment with **exogenous** glycosaminoglycans on growth and glycosaminoglycan synthesis of human

fibroblasts (WI-38) in culture.
AU Wever J; Schachtschabel D O; Sluke G; Wever G
SO MECHANISMS OF AGEING AND DEVELOPMENT, **(1980 Sep-Oct)** 14 (1-2) 89-99.
Journal code: LMJ. ISSN: 0047-6374.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198107
AB Short-term (several days) or long-term (several weeks and months) treatment of cultured human diploid fibroblasts (WI-38; phase II) with heparin at 20--500 micrograms/ml inhibited cell proliferation and stimulated glycosaminoglycan synthesis (as measured by the incorporation rates of [35S] sulfate and [14C] glucosamine into cellular and medium glycosaminoglycans). Characterization of the individual glycosaminoglycan types revealed an increased portion of incorporated radioactivity in the heparan sulfate and **hyaluronic acid** fractions of heparin-treated cells. Treatment with chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate of **hyaluronic acid** at concentrations up to 500 micrograms/ml exhibited no or slightly inhibitory (especially in the case of **hyaluronic acid**) effects on growth and glycosaminoglycan synthesis. The average cellular protein and RNA content of short- or long-term heparin (100 micrograms/ml)-treated cells was elevated by about 70--80%. "Senescent" (phase III) WI-38 cells exhibited a relative increase of [35S] sulfate and [14C] glucosamine incorporation into cell-bound and medium heparan sulfate. Possible mechanisms for the action of heparin (for example, interaction with specific cell-surface sites) and a potential role of heparan sulfate in the regulation of cell growth are discussed.
CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Division: DE, drug effects
Cell Survival
Cells, Cultured
***Fibroblasts: ME, metabolism**
*Glycosaminoglycans: BI, biosynthesis
Glycosaminoglycans: PD, pharmacology
*Heparin: PD, pharmacology
Heparitin Sulfate: BI, biosynthesis
Hyaluronic Acid: BI, biosynthesis
RN **9004-61-9 (Hyaluronic Acid)**; 9005-49-6 (Heparin); 9050-30-0 (Heparitin Sulfate)
CN 0 (Glycosaminoglycans)

L51 ANSWER 4 OF 4 MEDLINE
AN 79161249 MEDLINE
DN 79161249
TI Influence of **exogenous** glycosaminoglycans on growth and glycosaminoglycan synthesis of cultured human diploid fibroblasts (WI-38).
AU Schachtschabel D O; Wever J; Sluke G; Wever G
SO ZEITSCHRIFT FUR GERONTOLOGIE, **(1979 Jan-Feb)** 12 (1) 19-26.
Journal code: XXP. ISSN: 0044-281X.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197908
AB Human diploid fibroblast (WI-38) in monolayer culture were treated with exogenous glycosaminoglycans for short (up to 4 days) or long (several weeks and months) periods, and the effects on growth and glycosaminoglycan synthesis, as measured by the incorporation of 35S-sulfate and 14C-glycosamine into cell-bound and cell-released (medium) glycosaminoglycans, were determined. Short- and long-term exposure to chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate or **hyaluronic acid** at concentrations up to 100 microgram/ml did not affect cell growth, while heparin (between 20 and 100

micrograms/ml), heparan sulfate (above 100 micrograms/ml) or **hyaluronic acid** (2500 micrograms/ml) exerted significant growth-inhibitory effects. While short-term or long-term influence (each at 100 micrograms/ml) of chondroitin-4-sulfate, chondroitin-6-sulfate and **hyaluronic acid** resulted in a slight inhibition of incorporation of both radioactive precursors into cell-bound glycosaminoglycans, heparin (between 20 and 500 micrograms/ml) or heparan sulfate (at 100 or 500 micrograms/ml) significantly stimulated 14C-glycosamine incorporation into cell-bound glycosaminoglycans, what appeared to be predominantly into the **hyaluronic acid** fraction. Following long-term treatment with heparin at 20, 50 or 100 micrograms/ml, incorporation rates of both 14C-glucosamine and 35S-sulfate into both cell-bound and cell-released (medium) glycosaminoglycans were elevated, suggesting a general stimulation of glycosaminoglycan synthesis. Possible mechanisms for the action of these compounds (especially heparin) were discussed, e.g. an interaction with specific cell surface-associated sites.

CT Check Tags: Human; In Vitro
Cell Division
Cells, Cultured
Depression, Chemical
***Fibroblasts: DE, drug effects**
***Fibroblasts: ME, metabolism**
*Glycosaminoglycans: BI, biosynthesis
*Glycosaminoglycans: PD, pharmacology
*Growth: DE, drug effects
Proteins: AN, analysis
Time Factors

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=> fil biosis
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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RECORDS LAST ADDED: 5 April 2000 (20000405/ED)

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for details.

=> d his 152-

     (FILE 'MEDLINE' ENTERED AT 07:33:48 ON 08 APR 2000)

     FILE 'BIOSIS' ENTERED AT 07:57:54 ON 08 APR 2000
L52         6814 S L1 OR L2
L53         9108 S L6
L54         9123 S L52,L53
L55         7459 S L54 AND PY<=1996
                 E PILARSKI L/AU
L56          181 S E3-E8
L57           17 S L54 AND L56
L58            8 S L57 AND 00520/CC
L59            9 S L57 AND (CONGRESS? OR CONFERENCE? OR POSTER? OR SYMPOS? OR ME
L60            9 S L58,L59
L61            8 S L57 NOT L60

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L62           10 DUP REM L33 L61 (7 DUPLICATES REMOVED)

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L63            1 S L61 AND PREV199900001852/DN
L64           10 S L60,L63
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FILE 'BIOSIS' ENTERED AT 08:02:39 ON 08 APR 2000

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L64 ANSWER 1 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:274978 BIOSIS
DN PREV199900274978
TI Cellular redistribution of the **hyaluronan** (HA) receptor RHAMM is regulated by HA binding.
AU Gares, S. (1); Crainie, M. (1); **Pilarski, L. (1)**
CS (1) Univ. of Alberta, Edmonton, T6G 1Z2 Canada
SO FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A1134.
Meeting Info.: **Annual Meeting of the Professional Research Scientists on Experimental Biology 99** Washington, D.C., USA April 17-21, 1999
Federation of American Societies for Experimental Biology
. ISSN: 0892-6638.
DT **Conference**
LA English
CC Cytology and Cytochemistry - General *02502
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802
Immunology and Immunochemistry - General; Methods *34502
Metabolism - General Metabolism; Metabolic Pathways *13002
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
thymocytes: immune system
IT Chemicals & Biochemicals
hyaluronan: binding; nystatin; phospholipase C; RHAMM: cellular redistribution, **hyaluronan** receptor
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **9004-61-9 (HYALURONAN)**
9001-86-9 (PHOSPHOLIPASE C)
1400-61-9 (NYSTATIN)

L64 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:185172 BIOSIS
DN PREV199900185172
TI Potential role for **hyaluronan** (HA) and the HA receptor RHAMM in hematopoietic progenitor cell mobilization and trafficking.
AU **Pilarski, L. M. (1)**; Pruski, E.; Wizniak, J.; Paine, D.; Mant, M. J.; Beich, A. R.
CS (1) Dep. Oncol., Univ. Alberta, Edmonton, AB T6G 1Z2 Canada
SO **Proceedings of the American Association for Cancer Research Annual Meeting**, (March, 1999) Vol. 40, pp. 721.
Meeting Info.: **90th Annual Meeting of the American Association for Cancer Research** Philadelphia, Pennsylvania, USA April 10-14, 1999
American Association for Cancer Research
. ISSN: 0197-016X.
DT **Conference**
LA English
CC Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Cytology and Cytochemistry - Animal *02506

Biochemical Studies - Carbohydrates *10068
Biophysics - Membrane Phenomena *10508
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Mammalia - Unspecified 85700
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Tumor Biology
IT Parts, Structures, & Systems of Organisms
bone marrow: blood and lymphatics, immune system; hematopoietic progenitor cells: blood and lymphatics
IT Chemicals & Biochemicals
hyaluronan; RHAMM: **hyaluronan** receptor
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Mammalia: Vertebrata, Chordata, Animalia
ORGN Organism Name
mammal (Mammalia)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
RN **9004-61-9 (HYALURONAN)**

L64 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:97926 BIOSIS
DN PREV199900097926
TI Overexpression of the **hyaluronan** receptor RHAMM characterizes the malignant clone in multiple myeloma: Identification of three distinct RHAMM variants.
AU **Pilarski, Linda M. (1)**; Crainie, Mary; Mant, Michael J.; Belch, Andrew R.
CS (1) Dep. Oncol. and Med., Univ. Alberta, Edmonton, AB Canada
SO Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 257A.
Meeting Info.: **40th Annual Meeting of the American Society of Hematology** Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DT **Conference**
LA English
CC Genetics and Cytogenetics - Human *03508
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Genetics and Cytogenetics - Animal *03506
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
Neoplasms and Neoplastic Agents - General *24002
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae 86215
Muridae 86375
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Tumor Biology
IT Parts, Structures, & Systems of Organisms
plasma cell: blood and lymphatics, immune system; B cell: blood and lymphatics, immune system; B-chronic lymphocytic leukemia cells
IT Diseases
multiple myeloma: blood and lymphatic disease, immune system disease, neoplastic disease; B lymphoma: blood and lymphatic disease, neoplastic disease, immune system disease
IT Chemicals & Biochemicals
cDNA [complementary DNA]; RHAMM [receptor for **hyaluronan** receptor for mediated motility]: intracellular, transcripts; human RHAMM gene [human receptor for **hyaluronan** mediated motility gene] (Hominidae): splice variants
IT Alternate Indexing
Multiple Myeloma (MeSH)
IT Miscellaneous Descriptors

Meeting Abstract; Meeting Poster
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient; murine (Muridae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
RN **9004-61-9 (HYALURONAN)**

L64 ANSWER 4 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:1852 BIOSIS
DN **PREV199900001852**
TI Problems with RHAMM: A new link between surface adhesion and oncogenesis? (and reply.
AU Hofmann, Martin (1); Assmann, Volker; Fieber, Christina; Sleeman, Jonathan P.; Moll, Juergen; Ponta, Helmut; Hart, Ian R.; Herrlich, Peter; Turley, E. A.; **Pilarski, L.**; Nagy, J. I.
CS (1) Forschungszentrum Karlsruhe, Univ. Karlsruhe, Inst. Genetics D-76021 Karlsruhe Germany
SO Cell, (Nov. 25, 1998) Vol. 95, No. 5, pp. 591-593.
ISSN: 0092-8674.
DT Article
LA English
CC Biophysics - Membrane Phenomena *10508
Cytology and Cytochemistry - Human *02508
Biochemical Studies - General *10060
Neoplasms and Neoplastic Agents - General *24002
BC Hominidae 86215
IT Major Concepts
Membranes (Cell Biology)
IT Parts, Structures, & Systems of Organisms
receptor for **hyaluronic acid** mediated motility
IT Miscellaneous Descriptors
oncogenesis; surface adhesion
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **9004-61-9 (HYALURONIC ACID)**

L64 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:67881 BIOSIS
DN PREV199800067881
TI A central role for the Ras oncogene in RHAMM-mediated spread of myeloma.
AU Masellis, A. M. (1); Belch, A. R.; Mant, M. M.; **Pilarski, L. M.**
CS (1) Cross Cancer Inst., Edmonton AB Canada
SO Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 352A-353A.
Meeting Info.: **39th Annual Meeting of the American Society of Hematology** San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DT **Conference**
LA English
CC Neoplasms and Neoplastic Agents - General *24002
Cytology and Cytochemistry - General *02502
Genetics and Cytogenetics - General *03502
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Animalia - Unspecified 33000
IT Major Concepts
Tumor Biology

IT Parts, Structures, & Systems of Organisms
bone marrow: blood and lymphatics, malignant plasma cell accumulation, immune system
IT Diseases
multiple myeloma: blood and lymphatic disease, immune system disease, neoplastic disease
IT Chemicals & Biochemicals
Ras oncogene; Receptor for **Hyaluronan** Mediated Motility [RHAMM]
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Animalia
ORGN Organism Name
ANBL/6 (Animalia)
ORGN Organism Superterms
Animals
RN **9004-61-9 (HYALURONAN)**

L64 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:54007 BIOSIS
DN PREV199799353210
TI Isolation of cytokeratin 18 mRNA in RHAMM positive peripheral blood cells: Implications in migration of breast cancer epithelial cells and establishment of micrometastasis.
AU Masellis-Smith, Anna (1); MacDonald, Dawn M.; **Pilarski, Linda M.** ; Starreveld, Adalel
CS (1) Dep. Oncol., Radiation Oncol., Univ. Alberta, Edmonton, AB Canada
SO Blood, (1996) Vol. 88, No. 10 SUPPL. 1 PART 1-2, pp. 257A.
Meeting Info.: **Thirty-eighth Annual Meeting of the American Society of Hematology** Orlando, Florida, USA December 6-10, 1996
ISSN: 0006-4971.
DT **Conference; Abstract; Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Membrane Phenomena *10508
Movement *12100
Reproductive System - Pathology *16506
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004
Neoplasms and Neoplastic Agents - Biochemistry *24006
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology); Physiology; Reproductive System (Reproduction); Tumor Biology
IT Chemicals & Biochemicals
HYALURONAN
IT Miscellaneous Descriptors
BLOOD AND LYMPHATICS; BREAST CANCER; CELL MIGRATION; CYTOKERATIN 18; EPITHELIAL CELLS; HEMATOLOGY; MESSENGER RNA; MICROMETASTASIS; MRNA; NEOPLASTIC DISEASE; PERIPHERAL BLOOD CELLS; RECEPTOR FOR **HYALURONAN** MEDIATED MOTILITY; REPRODUCTIVE SYSTEM; REPRODUCTIVE SYSTEM DISEASE; RHAMM POSITIVE; TUMOR BIOLOGY
RN **9004-61-9 (HYALURONAN)**

L64 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:53387 BIOSIS
DN PREV199799352590
TI **Hyaluronan** induction of RAF kinase and MAP kinase in circulating B cells but not in bone marrow plasma cells of myeloma patients.
AU Masellis-Smith, Anna; Belch, Andrew R.; Ostergaard, Hanne; **Pilarski, Linda M.**
CS Dep. Oncology Med. Microbiol. Immunol., Univ. Alberta, Edmonton, AB USA

SO Blood, (1996) Vol. 88, No. 10 SUPPL. 1 PART 1-2, pp. 102A.
Meeting Info.: **Thirty-eighth Annual Meeting of the American Society of Hematology** Orlando, Florida, USA December 6-10, 1996
ISSN: 0006-4971.
DT **Conference; Abstract; Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biophysics - Membrane Phenomena *10508
Enzymes - Chemical and Physical *10806
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Neoplasms and Neoplastic Agents - Immunology *24003
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Clinical Immunology (Human Medicine, Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Membranes (Cell Biology); Oncology (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
HYALURONAN; KINASE; PROTEIN KINASE
IT Miscellaneous Descriptors
B CELLS; BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; BONE MARROW PLASMA CELL; CLINICAL IMMUNOLOGY; DISEASE PROGRESSION; HEMATOLOGY; **HYALURONAN**; IMMUNE SYSTEM DISEASE; IMMUNOGLOBULIN H; MAP KINASE; MEMBRANES; MITOGEN-ACTIVATED PROTEIN KINASE; MULTIPLE MYELOMA; NEOPLASTIC DISEASE; ONCOLOGY; PATIENT; RAF KINASE; SIGNAL TRANSDUCTION PATHWAY
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN **9004-61-9 (HYALURONAN)**
9031-44-1 (KINASE)
9026-43-1 (PROTEIN KINASE)

L64 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:307737 BIOSIS
DN PREV199699030093
TI **Hyaluronan** binding to human thymocytes is enhanced by anti-RHAMM antibodies.
AU Gares, S. (1); Turley, E.; **Pilarski, L.**
CS (1) Univ. Alberta, Edmonton, AB T6G 1Z2 Canada
SO FASEB Journal, (1996) Vol. 10, No. 6, pp. A1046.
Meeting Info.: **Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists** New Orleans, Louisiana, USA June 2-6, 1996
ISSN: 0892-6638.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and

Reticuloendothelial System *15008
Endocrine System - Thymus *17016
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Development; Endocrine System (Chemical Coordination and Homeostasis); Membranes (Cell Biology)
IT Chemicals & Biochemicals
HYALURONAN
IT Miscellaneous Descriptors
MEETING ABSTRACT; RECEPTOR FOR **HYALURONAN**-MEDIATED MOTILITY; THYMOCYTE DEVELOPMENT
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN **9004-61-9 (HYALURONAN)**

L64 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:47932 BIOSIS
DN PREV199698620067
TI Differential usage of RHAMM and CD44 during migration of B lineage cells in multiple myeloma.
AU Masellis-Smith, A. (1); Belch, A. R.; Turley, E. A.; Mant, M. J.; **Pilarski, L. M.**
CS (1) Dep. Oncology, Univ. Alberta, Edmonton, AB Canada
SO Blood, (1995) Vol. 86, No. 10 SUPPL. 1, pp. 62A.
Meeting Info.: **37th Annual Meeting of the American Society of Hematology** Seattle, Washington, USA December 1-5, 1995
ISSN: 0006-4971.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Carbohydrates 10068
Biophysics - Membrane Phenomena *10508
Movement *12100
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Development; Hematology (Human Medicine, Medical Sciences); Membranes (Cell Biology); Oncology (Human Medicine, Medical Sciences); Physiology
IT Chemicals & Biochemicals
HYALURONIC ACID
IT Miscellaneous Descriptors
HYALURONIC ACID RECEPTOR; **MEETING ABSTRACT** ; **MEETING POSTER**; TUMOR GROWTH
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN **9004-61-9 (HYALURONIC ACID)**

L64 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:382155 BIOSIS
DN PREV199598396455
TI Functional relation between beta-1 integrins and RHAMM, a receptor for **hyaluronan**-mediated motility on human thymocytes.
AU Gares, S. L.; McNeil, D.; **Pilarski, L. M.**
CS Univ. Alberta, Edmonton, AB Canada
SO 9TH INTERNATIONAL **CONGRESS** OF IMMUNOLOGY.. (1995) pp. 261. The 9th International **Congress** of Immunology.
Publisher: 9th International **Congress** of Immunology San Francisco, California, USA.
Meeting Info.: **Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies** San Francisco, California, USA July 23-29, 1995
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Developmental Biology - Embryology - Morphogenesis, General *25508
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Development
IT Chemicals & Biochemicals
INTEGRINS; **HYALURONAN**
IT Miscellaneous Descriptors
DEVELOPMENT; FIBRONECTIN; MATURATION; **MEETING ABSTRACT**
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 153-87-7QD (INTEGRINS)
60791-49-3QD (INTEGRINS)
9004-61-9 (HYALURONAN)

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(FILE 'BIOSIS' ENTERED AT 08:02:39 ON 08 APR 2000)
L65 1538 S L55 AND 00520/CC
L66 1925 S L55 AND (CONGRESS? OR CONFERENCE? OR POSTER? OR SYMPOS? OR ME
L67 1939 S L65,L66 NOT L64
L68 458 S L67 AND *02506/CC
L69 251 S L67 AND *02508/CC
L70 11 S L67 AND *02502/CC
L71 701 S L68-L70
L72 36 S L71 AND *15004/CC
L73 1 S L72 AND POLYSULFAT?/TI
L74 86 S L71 AND (*12512 OR 220?)/CC
L75 5 S L74 AND MOLECULAR WEIGHT
L76 1 S L74 AND MICROCIRCULATION
L77 55 S 11107/CC AND L71
L78 1 S L76 AND L77
L79 2 S L77 AND (VIVO AND VITRO)
L80 1 S L79 AND MODULATE
L81 8 S L73,L75,L76,L78,L80 NOT L57

=> d all tot

L81 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:200466 BIOSIS
DN PREV199698756595
TI Comparison of protective efficacy in different **molecular weight** of **sodium hyaluronates** on the corneal endothelium during phacoemulsification.
AU Negishi, K. (1); Bissen-Miyajima, H.; Tsubota, K.
CS (1) Dep. Ophthalmol., Natl. Saitama Hosp., Saitama Japan
SO Investigative Ophthalmology & Visual Science, (1996) Vol. 37, No. 3, pp. S83.
Meeting Info.: **1996 Annual Meeting of the Association for Research in Vision and Ophthalmology** Fort Lauderdale, Florida, USA April 21-26, 1996
ISSN: 0146-0404.
DT **Conference**
LA English
CC **Cytology and Cytochemistry - Animal *02506**
Biochemical Studies - General 10060
Biochemical Studies - Minerals 10069
Biophysics - Molecular Properties and Macromolecules *10506
Anatomy and Histology, General and Comparative - Experimental Anatomy *11104
Pathology, General and Miscellaneous - Therapy *12512
Sense Organs, Associated Structures and Functions - Physiology and Biochemistry *20004
Pharmacology - Sense Organs, Associated Structures and Functions *22031
BC Suidae *85740
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Morphology; Pathology; Pharmacology; Sense Organs (Sensory Reception)
IT Chemicals & Biochemicals
SODIUM HYALURONATES; SODIUM HYALURONATE
IT Miscellaneous Descriptors
MEETING ABSTRACT; MEETING POSTER; OPHTHALMIC-DRUG; **SODIUM HYALURONATE**
ORGN Super Taxa
Suidae: Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
pig (Suidae)
ORGN Organism Superterms
animals; artiodactyls; chordates; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
RN 9067-32-7D (**SODIUM HYALURONATES**)
9067-32-7 (**SODIUM HYALURONATE**)

L81 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:520562 BIOSIS
DN PREV199598534862
TI Long term protective effect of a high **molecular weight hyaluronic acid** (HA) in an animal model of articular cartilage injury.
AU Plaza, V. L. (1); Rayan, V.; Thonar, E. J.-M. A.; Williams, J. M.
CS (1) Dep. Anat., Rush Med. Coll. Rush Presbyterian, St. Luke's Med. Cent., Chicago, IL 60612 USA
SO Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S161.
Meeting Info.: **59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals** San Francisco, California, USA October 21-26, 1995
ISSN: 0004-3591.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**

Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Bones, Joints, Fasciae, Connective and Adipose Tissue - Anatomy *18002
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
BC Leporidae *86040
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology); Metabolism; Pathology; Pharmacology; Skeletal System (Movement and Support)
IT Chemicals & Biochemicals
HYALURONIC ACID
IT Miscellaneous Descriptors
ANTIARTHRITIC-DRUG; HIGH **MOLECULAR WEIGHT HYALURONIC ACID**; MATRIX PROTEOGLYCAN RESYNTHESIS; **MEETING ABSTRACT**; **MEETING POSTER**; OSTEOARTHRITIS; PHARMACODYNAMICS; POTENTIAL TREATMENT INTERVENTION
ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rabbit (Leporidae)
ORGN Organism Superterms
animals; chordates; lagomorphs; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
RN **9004-61-9 (HYALURONIC ACID)**

L81 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:200699 BIOSIS
DN PREV199598214999
TI Protection of corneal endothelium by **hyaluronic acids** with different **molecular weights**.
AU Ohyama, M.; Shimazaki, J.; Yang, H. Y.; Toda, I.; Fujishima, H.; Tsubota, K.
CS Dep. Ophthalmol., Tokyo Dental College, Chiba Japan
SO Investigative Ophthalmology & Visual Science, (1995) Vol. 36, No. 4, pp. S135.
Meeting Info.: **Annual Meeting of the Association for Research in Vision and Ophthalmology** Fort Lauderdale, Florida, USA May 14-19, 1995
ISSN: 0146-0404.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Anatomy and Histology, General and Comparative - Surgery *11105
Metabolism - Carbohydrates *13004
Cardiovascular System - Blood Vessel Pathology *14508
Sense Organs, Associated Structures and Functions - Pathology *20006
Pharmacology - Sense Organs, Associated Structures and Functions *22031

BC Leporidae *86040
IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Cell Biology; Metabolism; Pharmacology; Sense Organs (Sensory Reception); Surgery (Medical Sciences)
IT Chemicals & Biochemicals
HYALURONIC ACIDS
IT Miscellaneous Descriptors
ENDOTHELIAL CELL DAMAGE; HEALON; **MEETING ABSTRACT**; **MEETING POSTER**; OPEGAN; OPHTHALMIC-DRUG; SURGERY
ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rabbit (Leporidae)
ORGN Organism Superterms
animals; chordates; lagomorphs; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
RN 9004-61-9D (**HYALURONIC ACIDS**)

L81 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:4710 BIOSIS
DN PREV199598019010
TI Intra-articular injection of high **molecular weight hyaluronate** inhibits type II collagen-induced arthritis in monkeys, an experimental model of rheumatoid arthritis.
AU Fujii, Katsuyuki; Ukari, Yoshikazu; Ohashi, Toshiko; Murota, Kagehisa
CS Jikei Univ. Sch. Med., Tokyo 105 Japan
SO Arthritis & Rheumatism, (1994) Vol. 37, No. 9 SUPPL., pp. S339.
Meeting Info.: **58th National Scientific Meeting of the American College of Rheumatology and the 29th National Scientific Meeting of the Association of Rheumatology Health Professionals** Minneapolis, Minnesota, USA October 23-27, 1994
ISSN: 0004-3591.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Microscopy Techniques - Histology and Histochemistry *01056
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - General *17002
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
Routes of Immunization, Infection and Therapy *22100
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Primates - Unspecified *86190
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Immune System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Pathology; Pharmacology; Skeletal System (Movement and Support)

IT Chemicals & Biochemicals
HYALURONATE; STROMELYSIN
IT Miscellaneous Descriptors
ANIMAL MODEL; ANTIARTHRITIC-DRUG; ANTIINFLAMMATORY-DRUG; CHONDROCYTE; COLLAGEN; HIGH **MOLECULAR WEIGHT HYALURONATE** ; IMMUNOHISTOCHEMISTRY; INTERLEUKIN-1; **MEETING ABSTRACT**; **MEETING POSTER**; STROMELYSIN; TUMOR NECROSIS FACTOR
ORGN Super Taxa
Primates - Unspecified: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Primates (Primates - Unspecified)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; nonhuman primates; primates; vertebrates
RN **9004-61-9 (HYALURONATE)**
79955-99-0 (STROMELYSIN)

L81 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:430112 BIOSIS
DN PREV199497443112
TI Synthetic **polysulfated hyaluronic acid** is a potent inhibitor for tumor necrosis factor production.
AU Chang, N.-S. (1); Armand, G.
CS (1) Guthrie Res. Inst., Sayre, PA USA
SO Journal of Leukocyte Biology, (1994) Vol. 0, No. SUPPL., pp. 19.
Meeting Info.: **Thirtieth National Meeting of the Society for Leukocyte Biology** Tucson, Arizona, USA September 21-24, 1994
ISSN: 0741-5400.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - General *17002
BC Animalia - Unspecified *33000
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
HYALURONIC ACID
IT Miscellaneous Descriptors
LEUKOCYTE; **MEETING ABSTRACT**
ORGN Super Taxa
Animalia - Unspecified: Animalia
ORGN Organism Name
animal (Animalia - Unspecified); Animalia (Animalia - Unspecified)
ORGN Organism Superterms
animals
RN **9004-61-9 (HYALURONIC ACID)**

L81 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:237478 BIOSIS
DN PREV199497250478
TI Low **molecular weight sodium hyaluronate** prevents major basic protein inhibition of epithelial migration.
AU Trocme, S. D. (1); Hallberg, C. K. (1); Gleich, G. J.
CS (1) Dep. Ophthalmol., Univ. Texas Med. Branch, Galveston, TX USA

SO Investigative Ophthalmology & Visual Science, (1994) Vol. 35, No. 4, pp. 1943.
Meeting Info.: **Annual Meeting of the Association for Research in Vision and Ophthalmology** Sarasota, Florida, USA May 1-6, 1994
ISSN: 0146-0404.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Proteins, Peptides and Amino Acids *13012
Sense Organs, Associated Structures and Functions - Physiology and Biochemistry *20004
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Metabolism; Pathology; Sense Organs (Sensory Reception)
IT Chemicals & Biochemicals
SODIUM HYALURONATE
IT Miscellaneous Descriptors
MEETING ABSTRACT; MEETING POSTER
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9067-32-7 (SODIUM HYALURONATE)**

L81 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1990:272805 BIOSIS
DN BR39:4651
TI ACTIONS OF **HYALURONIC ACID** ON THE **MICROCIRCULATION** DURING WOUND HEALING.
AU KING S R; HICKERSON W L; PROCTOR K G
CS DEP. PHYSIOL., UNIV. TENN. HEALTH SCI. CENT., MEMPHIS, TENN. 38163, USA.
SO 74TH ANNUAL **MEETING** OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, PART II, WASHINGTON, D.C., USA, APRIL 1-5, 1990.
FASEB (FED AM SOC EXP BIOL) J. (1990) 4 (4), A1257.
CODEN: FAJOEC. ISSN: 0892-6638.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Carbohydrates 10068
Anatomy and Histology, General and Comparative - Regeneration and Transplantation *11107
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Pathology, General and Miscellaneous - Therapy 12512
Cardiovascular System - Physiology and Biochemistry *14504
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Integumentary System - Pathology *18506
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Cardiovascular System *22010
Pharmacology - Integumentary System, Dental and Oral Biology *22020
Developmental Biology - Embryology - Morphogenesis, General *25508

BC Hominidae 86215
Cricetidae 86310
IT Miscellaneous Descriptors
ABSTRACT HAMSTER CHEEK POUCH BURN PATIENTS INTRAVASCULAR GRANULOCYTES ANGIOGENESIS INFLAMMATORY CELLS HEALON CARDIOVASCULAR-DRUG DERMATOLOGICAL-DRUG
RN **9004-61-9 (HYALURONIC ACID)**

L81 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1987:369111 BIOSIS
DN BR33:59586
TI **HYALURONIC ACID** AND ITS DEGRADATION PRODUCTS **MODULATE** ANGIOGENESIS IN-**VIVO** AND IN-**VITRO**.
AU KUMAR S; WEST D
CS CHRISTIE HOSP. AND HOLT RADIUM INST., MANCHESTER M20 9BX, ENGL.
SO RIFKIN, D. B. AND M. KLAGSBRUN (ED.). CURRENT COMMUNICATIONS IN MOLECULAR BIOLOGY: ANGIOGENESIS: MECHANISMS AND PATHOBIOLOGY. IX+161P. COLD SPRING HARBOR LABORATORY: COLD SPRING HARBOR, NEW YORK, USA. ILLUS. PAPER. (1987) 0 (0), 90-94.
ISBN: 0-87969-300-2.
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Carbohydrates 10068
Biophysics - Membrane Phenomena *10508
Anatomy and Histology, General and Comparative - Regeneration and Transplantation *11107
Cardiovascular System - Physiology and Biochemistry *14504
In Vitro Studies, Cellular and Subcellular 32600
BC Bovidae 85715
IT Miscellaneous Descriptors
BOVINE ENDOTHELIAL CELL CHORIOALLANTOIC MEMBRANE
RN **9004-61-9 (HYALURONIC ACID)**

=> fil ca
FILE 'CA' ENTERED AT 08:41:54 ON 08 APR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1967 - 7 Apr 2000 VOL 132 ISS 16
FILE LAST UPDATED: 7 Apr 2000 (20000407/ED)

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=> d his 182-

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     (FILE 'BIOSIS' ENTERED AT 08:02:39 ON 08 APR 2000)

     FILE 'HCAPLUS' ENTERED AT 08:20:55 ON 08 APR 2000
L82         7689 S L1 OR L2
L83        10188 S L6
L84        10509 S L82,L83
               E PILARSKI L/AU
L85           65 S E3-E7
L86           10 S L84 AND L85

     FILE 'CA' ENTERED AT 08:22:55 ON 08 APR 2000
               E PILARSKI L/AU
L87           62 S E3-E8
L88        10319 S L84
L89            9 S L87 AND L88
L90            2 S L89 AND P/DT
L91         8665 S L88 AND (PY<=1996 OR PRY<=1996 OR PRY.B<=1996 OR AY<=1996 OR
L92          109 S L91 AND (HEMATOPOIE? OR HAEMATOPOIE? OR (STEM OR MAST OR DEND
L93           84 S L91 AND ERYTHROCYT?
L94          146 S L91 AND PLATELET
L95           37 S L91 AND (STEM OR MAST OR DENDRITIC OR PROGENITOR)(L)CELL#/CW
               E CELL/CW
L96        24259 S E3,E26 (L) (STEM OR HEMATOPOIET? OR DENDRITIC OR RED OR MAST
L97           46 S L91 AND L96
L98          322 S L92-L95,L97 NOT L90
L99          144 S L98 AND (1 OR 15 OR 63)/SC,SX
L100          40 S L99 AND (L1 (L) (THU/RL OR USES/RL) OR L2 (L) (THU/RL OR USE
L101           8 S L100 AND (CULTURE OR MAGAKARYOCYT? OR RESPONS? OR REGENERATIO
L102          10 S L90,L101
L103         104 S L99 NOT L100,L102
L104          22 S L103 AND P/DT
L105           1 S L104 AND EXOGENOUS
L106          11 S L102,L105

     FILE 'CA' ENTERED AT 08:41:54 ON 08 APR 2000

=> d all tot l106

L106 ANSWER 1 OF 11  CA  COPYRIGHT 2000 ACS
AN   131:722  CA
TI   Methods for cell mobilization using in vivo treatment with
     hyaluronan, and therapeutic methods
IN   Pilarski, Linda May
PA   Hyal Pharmaceutical Corporation, Can.
SO   Can. Pat. Appl., 60 pp.
     CODEN: CPXXEB
DT   Patent
LA   English
IC   ICM  A61K031-725
CC   1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   CA 2199756         AA   19980912      CA 1997-2199756  19970312
AB   The use of forms of hyaluronic acid having a mol. wt.
     less than about 750,000 daltons, selected from hyaluronic
     acid and pharmaceutically acceptable salts thereof, is provided
     for the same purposes known for using recombinant GM-CSF or G-CSF.  The
     methods of the invention use exogenous forms of hyaluronic
     acid for mobilizing hematopoietic cells to the circulation,
     enabling various methods of treatment (cancer treatment, organ
     transplantation, etc.).
ST   hyaluronic acid cell mobilization therapeutic;
     hyaluronan cell mobilization therapeutic; hematopoietic cell
     mobilization hyaluronan; cancer treatment hematopoietic cell
```

mobilization **hyaluronan**; organ transplant hematopoietic cell mobilization **hyaluronan**

IT Neoplasm
(cell, release from bone marrow and other tissue into blood; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Cytotoxic agents
(cytoreductive therapy before hematopoietic cell transplant; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Immunity
(disorder, immune reactivity-damaging conditions; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Allergy inhibitors
Antiasthmatics
Antitumor agents
Autoimmune disease
B cell (lymphocyte)
Bone marrow
Dendritic cell
Drug delivery systems
Erythroblast
Erythrocyte
Hematopoiesis
Hematopoietic precursor cell
Monocyte
Polymorphonuclear leukocyte
T cell (lymphocyte)
Transplant and Transplantation
Transplant rejection
(**hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Immunosuppressants
(immunosuppressive regimen optimization; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Hematopoietic precursor cell
(mast cell; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Lymphocyte
(plasma cell; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Cell
(stem; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Bone marrow
(stroma, stromal cell; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT Immunosuppression
(treatment of chemotherapy-induced; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT AIDS (disease)
Chemotherapy
(treatment of immunosuppression from; **hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT **9004-61-9, Hyaluronic acid 9067-32-7**
, Sodium hyaluronate
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

IT 11096-26-7, Erythropoietin 83869-56-1, GM-CSF 143011-72-7, G-CSF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**hyaluronic acid** for hematopoietic cell mobilization, and therapeutic methods)

L106 ANSWER 2 OF 11 CA COPYRIGHT 2000 ACS
AN 129:62970 CA
TI Treatment of disease and conditions associated with **macrophage** infiltration
IN Turley, Eva Anne; Asculai, Samuel Simon
PA Hyal Pharmaceutical Corp., Can.
SO U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 675,908.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-70
NCL 514054000
CC **1-8** (Pharmacology)
Section cross-reference(s): **63**
FAN.CNT 21

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5767106	A	19980616	US 1994-295390	19940825	<--
	US 5827834	A	19981027	US 1994-286263	19940805	<--
	CA 2130762	AA	19960225	CA 1994-2130762	19940824	<--
	US 5811410	A	19980922	US 1995-465335	19950605	<--
	US 5830882	A	19981103	US 1995-462615	19950605	<--
	US 5852002	A	19981222	US 1995-462147	19950605	<--
	HU 76895	A2	19971229	HU 1997-1518	19950802	<--
	ZA 9507056	A	19960326	ZA 1995-7056	19950823	<--
	CN 1131539	A	19960925	CN 1995-116616	19950823	<--
	WO 9817320	A1	19980430	WO 1996-CA700	19961018	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9672721	A1	19980515	AU 1996-72721	19961018	<--
	EP 952855	A1	19991103	EP 1996-934250	19961018	<--
	R: DE, FR, GB, IT, SE					

PRAI US 1991-675908 19910520 <--
US 1992-838673 19920221 <--
US 1994-200309 19940223 <--
CA 1994-2130762 19940824 <--
CA 1989-612307 19890921 <--
WO 1996-CA700 19961018 <--

AB A method of treating a human having a disease or condition characterized by macrophage, neutrophil, or other white blood cell infiltration into the area damaged by the disease or condition is disclosed, the method comprising administering to the human an effective amt. of **hyaluronic acid** and/or salts thereof for a period of time until the administration is no longer required.

ST macrophage infiltration disease therapy **hyaluronate**
IT Macrophage
(infiltration; treatment of disease and conditions assocd. with macrophage infiltration)
IT Injections (drug delivery systems)
Leukocyte infiltration
Myocardial infarction
Nonsteroidal anti-inflammatory drugs
Platelet aggregation inhibitors
Stroke
.beta.-Adrenoceptor antagonists
(treatment of disease and conditions assocd. with macrophage infiltration)
IT **9004-61-9, Hyaluronic acid 9004-61-9D**
, **Hyaluronic acid**, salts **9067-32-7,**

Sodium hyaluronate
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); **USES (Uses)**
(treatment of disease and conditions assocd. with macrophage infiltration)

IT 50-78-2, Aspirin 9002-01-1, Streptokinase 9005-49-6, Heparin, biological studies 105913-11-9, Plasminogen activator
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(treatment of disease and conditions assocd. with macrophage infiltration)

L106 ANSWER 3 OF 11 CA COPYRIGHT 2000 ACS
AN 127:298795 CA
TI Promotion of **regeneration** of organized tissues
IN Hansson, Hans-Arne
PA Hansson, Hans-Arne, Swed.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-06
ICS A61L031-00; A61F002-04
CC **63-7** (Pharmaceuticals)
Section cross-reference(s): **1**

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9737002	A1	19971009	WO 1997-SE565	19970401	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2248729	AA	19971009	CA 1997-2248729	19970401	<--
AU 9723157	A1	19971022	AU 1997-23157	19970401	<--
BR 9708459	A	19990413	BR 1997-8459	19970401	<--
CN 1219965	A	19990616	CN 1997-195054	19970401	<--
EP 942960	A1	19990922	EP 1997-915831	19970401	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
NO 9804534	A	19981125	NO 1998-4534	19980928	<--

PRAI SE 1996-1243 19960329 <--
WO 1997-SE565 19970401

AB The invention relates to system, method and device for promoting growth of tissue regenerate into a wound area in an organized tissue structure in a living human or animal body from a wound surface of the wound area in a predetd. direction. An encasement structure encases the wound area to inhibit ingress of granulation tissue to the wound area and mech. guide means for the outgrowing tissue regenerate are disposed in the encased wound area so as to extend in the predetd. direction. In one aspect a fibrin network formation inhibiting agent is concomitantly administered to the wound surface of the encased wound area. In another aspect the mech. guide means takes the form of a gel structure provided with one or more guide channels for the outgrowing tissue regenerate which extend in the predetd. direction.

ST regeneration tissue fibrin network formation inhibitor

IT Joint (anatomical)
(capsule, tissue regeneration promotion in; promotion of regeneration of organized tissues)

IT Neurotrophic factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ciliary; promotion of regeneration of organized tissues)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-; promotion of regeneration of organized tissues)
IT Skin
(endothelial cells; promotion of regeneration of organized tissues)
IT Cell (biological)
(inflammatory; promotion of regeneration of organized tissues)
IT Fibrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(network formation inhibitors; promotion of regeneration of organized tissues)
IT Growth factors (animal)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroglia growth factors; promotion of regeneration of organized tissues)
IT Pumps
(osmotic; promotion of regeneration of organized tissues)
IT Physiological saline solutions
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphate-buffered; promotion of regeneration of organized tissues)
IT Animal tissue
Fibrinolytics
Fibroblast
Filaments
Macrophage
Nonwoven fabrics
Prosthetic implants
Schwann cell
Wound healing (animal)
Wound healing promoters
(promotion of regeneration of organized tissues)
IT Collagens, biological studies
Fibers
Hydrogels
Lipids, biological studies
Physiological saline solutions
Platelet-derived growth factors
Polyamide fibers, biological studies
Polyamides, biological studies
Polymers, biological studies
Polysaccharides, biological studies
Polysiloxanes, biological studies
Proteins (general), biological studies
Sulfated oligosaccharides
Sulfated polysaccharides
Thrombin inhibitors
Transforming growth factor .alpha.
Transforming growth factors .beta.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(promotion of regeneration of organized tissues)
IT Bone
Cartilage
Ligament
Muscle
Nerves
Tendon
(tissue regeneration promotion in; promotion of regeneration of organized tissues)
IT 9002-18-0, Agar 9004-67-5, Methylcellulose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gel; promotion of regeneration of organized tissues)
IT 9001-29-0, Factor X
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; promotion of regeneration of organized tissues)
IT 1398-61-4, Chitin 7732-18-5, Water, biological studies 8001-27-2, Hirudin 9002-01-1, Streptokinase 9002-88-4, Polyethylene

9004-61-9, Hyaluronan 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9035-81-8, Trypsin inhibitor 9039-53-6, Urokinase 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24937-78-8, Ethylene-vinyl acetate copolymer 24967-94-0, Dermatan sulfate 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26780-50-7, Vicryl 36655-86-4, Polyglucuronic acid 37205-61-1, Protease inhibitor 52352-27-9, Polyhydroxybutyric acid 62031-54-3, Fibroblast Growth factor 62229-50-9, EGF 67763-96-6, Insulin-like Growth factor I 67763-97-7, Insulin-like Growth factor II 80181-31-3 105857-23-6, Actilyse 105913-11-9, Plasminogen activator 119978-18-6, Matrigel 120366-16-7, Biomatrix 155415-08-0, InoGatran 159776-70-2, MelaGatran
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(promotion of regeneration of organized tissues)

L106 ANSWER 4 OF 11 CA COPYRIGHT 2000 ACS
AN 127:283374 CA
TI Methods for cell mobilization using in vivo treatment with **hyaluronan** (ha)
IN **Pilarski, Linda May**
PA Hyal Pharmaceutical Corporation, Can.; Pilarski, Linda May
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-725
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9733592	A1	19970918	WO 1997-CA172	19970312
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2173272	AA	19971003	CA 1996-2173272	19960402
AU 9720888	A1	19971001	AU 1997-20888	19970312
EP 914133	A1	19990512	EP 1997-906061	19970312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-13401 19960314
CA 1996-2173272 19960402
WO 1997-CA172 19970312

AB The use of forms of **hyaluronic acid** having a mol. wt. less than about 750,000 daltons selected from the group consisting of **hyaluronic acid** and pharmaceutically acceptable salts thereof is provided for the same purposes known for using recombinant GM-CSF or G-CSF.
ST **hyaluronan** cell mobilization
IT Anemia (disease)
Animal cells
Antitumor agents
Autoimmune diseases
Fertility (animal)
Hematopoietic precursor cell
Immunosuppressants
Osteoporosis
Transplant (organ)

(cell mobilization using in vivo treatment with **hyaluronan**)

IT **9004-61-9, Hyaluronic acid 9067-32-7**
, Sodium hyaluronate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cell mobilization using in vivo treatment with **hyaluronan**)

L106 ANSWER 5 OF 11 CA COPYRIGHT 2000 ACS
AN 127:185860 CA
TI Cooperative combinations of ligands in a matrix to enhance wound healing and induce tissue **regeneration**
IN Vuori, Kristiina; Ruoslahti, Erkki I.
PA La Jolla Cancer Research Center, USA
SO U.S., 21 pp. Cont.-in-part of U.S. Ser. No. 176,999, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-00
NCL 514002000
CC **1-12** (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5654267	A	19970805	US 1994-347942	19941130	<--
	US 5830504	A	19981103	US 1995-456878	19950601	<--
	US 5955578	A	19990921	US 1995-463835	19950605	<--
	WO 9616983	A1	19960606	WO 1995-US15542	19951130	<--
	W: AU, CA, JP, KR					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	CA 2206175	AA	19960606	CA 1995-2206175	19951130	<--
	AU 9644123	A1	19960619	AU 1996-44123	19951130	<--
	EP 797584	A1	19971001	EP 1995-942948	19951130	<--
	R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE					
	JP 10509980	T2	19980929	JP 1995-519043	19951130	<--

PRAI US 1988-286973 19881220 <--
US 1992-978054 19921118 <--
US 1993-142842 19931025 <--
US 1994-176999 19940103 <--
US 1993-13154 19930201 <--
US 1994-347942 19941130 <--
US 1995-383616 19950202 <--
WO 1995-US15542 19951130 <--

AB A compn. for promoting cell migration and tissue regeneration contains a ligand for .alpha.v.beta.3 integrin and a ligand for the insulin receptor, the PDGF receptor, the IL-4 receptor, or the insulin-like growth factor (IGF) receptor, combined in a matrix. The .alpha.v.beta.3 integrin ligand may be vitronectin or a peptide contg. the sequence Arg-Gly-Asp or D-Arg-Gly-Asp. The matrix is preferably a biodegradable polymer such as **hyaluronic acid**, chondroitin sulfate, heparin, polylactate, starch, or collagen conjugated to the .alpha.v.beta.3 integrin ligand. The combination of .alpha.v.beta.3 ligand and growth factor produces an unexpected synergistic effect in enhancing wound healing compared with the effect of each component sep. Thus, human foreskin fibroblasts responded to PDGF with .apprx.2.3-fold higher DNA synthesis when plated on vitronectin than when plated on collagen.

ST integrin ligand wound healing; growth factor receptor tissue regeneration

IT Cell migration
Mitogens
Regeneration (animal)
Synergistic drug interactions
Wound healing promoters
(cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Interleukin 4
Platelet-derived growth factors

Vitronectin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Ligands
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for .alpha.v.beta.3 integrin; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Grb2 protein
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(insulin receptor substrate 1 protein assocn. with; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligands for .alpha.v.beta.3 integrins; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Insulin receptors
Insulin-like growth factor receptors
Integrin .alpha.v.beta.3
Interleukin 4 receptors
Platelet-derived growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligands for; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Collagens, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix, conjugates with growth factors; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT Insulin receptor substrate 1
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha.v.beta.3 integrin assocn. with; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT 9004-10-8, Insulin, biological studies 61912-98-9, Insulin-like growth factor 99896-85-2 120103-84-6 133656-20-9
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT 115926-52-8
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(insulin receptor substrate 1 protein assocn. with; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

IT **9004-61-9D**, **Hyaluronic acid**, conjugates with growth factors 9005-25-8D, Starch, conjugates with growth factors 9005-49-6D, Heparin, conjugates with growth factors 9007-28-7D, Chondroitin sulfate, conjugates with growth factors 9050-30-0D, Heparan sulfate, conjugates with growth factors 26009-03-0D, Poly(glycolic acid), conjugates with growth factors 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5D, Poly(glycolic acid), conjugates with growth factors
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(matrix; cooperative combinations of ligands in matrix to enhance wound healing and induce tissue regeneration)

L106 ANSWER 6 OF 11 CA COPYRIGHT 2000 ACS
AN 127:62875 CA
TI **Culture** of bone marrow **stem cells** partially

or completely differentiated into connective tissue cells in a three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** derivative

IN Abatangelo, Giovanni; Callegaro, Lanfranco

PA Fidia Advanced Biopolymers S.R.L., Italy; Abatangelo, Giovanni; Callegaro, Lanfranco

SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L027-00
ICS A61L015-28; C12N005-00

CC 9-11 (Biochemical Methods)
Section cross-reference(s): **63**

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9718842	A1	19970529	WO 1996-EP5093	19961119	<--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CA 2238011	AA	19970529	CA 1996-2238011	19961119	<--
	AU 9676934	A1	19970611	AU 1996-76934	19961119	<--
	AU 709236	B2	19990826			
	EP 863776	A1	19980916	EP 1996-939845	19961119	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO					
	JP 2000500372	T2	20000118	JP 1997-519385	19961119	<--

PRAI IT 1995-PD225 19951120 <--
WO 1996-EP5093 19961119 <--

AB A biol. material useful in skin grafts consists of (A) an efficient culture of autologous or homologous bone marrow **stem cells** partially or completely differentiated into connective tissue-specific cells, and the extracellular matrix secreted by these cells (or alternatively the extracellular matrix secreted by bone marrow **stem cells** partially or completely differentiated into a specific connective tissue or by the specific homologous mature connective tissue cells, said extracellular matrix being free from any cellular component) and (B) a 3-dimensional biocompatible and biodegradable matrix consisting of a **hyaluronic acid** deriv. Matrix (B) is free of immunogenic nonautologous proteins which might cause an immunol. reaction against the graft. Thus, a 3-dimensional nonwoven matrix of Hyaff 11 (benzyl **hyaluronate**) was seeded with human fibroblasts obtained from cultures of bone marrow mesenchymal **stem cells** and incubated in culture medium for 7-21 days to produce an artificial dermis. During incubation, the fibroblasts deposited an extracellular matrix contg. collagen types I, III, and IV, fibronectin, and laminin.

ST skin graft **hyaluronate** matrix fibroblast; bone marrow cell skin transplant; connective tissue cell skin transplant

IT Vascular endothelium
(cells of; culture of bone marrow **stem cells** differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** deriv.)

IT Adipocyte
Biodegradable materials
Bone marrow
Chondrocyte
Connective tissue **cells**
Extracellular matrix
Fibroblast

Keratinocyte
Myoblast
Nonwoven fabrics
Osteoblast
Skin transplant
Tissue culture (animal)
(culture of bone marrow **stem cells** differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** deriv.)

IT Collagens, biological studies
Fibronectins
Laminins
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(culture of bone marrow **stem cells** differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** deriv.)

IT Mesenchyme
(**stem cell**; culture of bone marrow **stem cells** differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** deriv.)

IT **9004-61-9D, Hyaluronic acid**, derivs.
9004-61-9D, Hyaluronic acid, esters
111744-92-4, Benzyl **hyaluronate**
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(culture of bone marrow **stem cells** differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of **hyaluronic acid** deriv.)

L106 ANSWER 7 OF 11 CA COPYRIGHT 2000 ACS
AN 125:105165 CA
TI Cooperative combinations of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue **regeneration**
IN Vuori, Kristiina; Ruoslahti, Erkki I.
PA La Jolla Cancer Research Foundation, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K007-08
ICS C07K014-49; C07K014-54; C07K014-62; C07K014-65; C07K014-78; C07K017-02; C07K017-10; A61K009-00; A61K038-10; A61K038-18; A61K038-20; A61K038-28; A61K038-30; A61K038-39
CC **1-12** (Pharmacology)
Section cross-reference(s): 2
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616983	A1	19960606	WO 1995-US15542	19951130 <--
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5654267	A	19970805	US 1994-347942	19941130 <--
	AU 9644123	A1	19960619	AU 1996-44123	19951130 <--
	EP 797584	A1	19971001	EP 1995-942948	19951130 <--
	R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
	JP 10509980	T2	19980929	JP 1995-519043	19951130 <--

PRAI US 1994-347942 19941130 <--
US 1988-286973 19881220 <--
US 1992-978054 19921118 <--
US 1993-142842 19931025 <--
US 1994-176999 19940103 <--
WO 1995-US15542 19951130 <--

AB Compns. and methods are provided for promoting cell migration and tissue

regeneration. The compns. contain a ligand for the .alpha.v.beta.3 integrin and a ligand for the insulin receptor, the PDGF receptor, the IL-4 receptor, or the IGF receptor, combined in a matrix. The combination of .alpha.v.beta.3 ligand and growth factor produces an unexpected synergistic effect in enhancing wound healing compared with the effect of each component sep. The present invention also provides a method of wound healing and a method of including tissue regeneration by applying the compns. of the present invention to the site of the wound.

ST integrin ligand growth factor wound healing; tissue regeneration integrin ligand growth factor

IT Wound healing
(cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Fibroblast
(effect of ligand binding of .alpha.v.beta.3 integrin on DNA synthesis in PDGF-stimulated human foreskin fibroblasts)

IT Animal tissue
(regeneration; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Ligands
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to .alpha.v.beta.3 integrin; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Grb-2, Grb-2 and phosphatidylinositol 3-kinase assocn. with IRS-1)

IT Phosphoproteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IRS-1 (insulin receptor substrate 1), p185/IRS-1 assocn. with .alpha.v.beta.3 integrin)

IT Animal growth regulator receptors
Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood **platelet**-derived growth factor, ligand for; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood **platelet**-derived growth factors, and analogs; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Pancreas, neoplasm
(carcinoma, integrin-IRS-1 assocn. in insulin-stimulated human pancreatic carcinoma cells)

IT Ligands
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated, cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Collagens, biological studies
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with .alpha.v.beta.3 integrin ligands; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Pharmaceutical dosage forms
(gels, synthetic matrix semi-gel; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(insulin, ligand for; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(insulin-like growth factor, ligand for; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Lymphokines and Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 4, and analogs; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Lymphokine and cytokine receptors
Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 4, ligand for; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Drug interactions
(synergistic, cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitronectins, cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT Integrins
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.alpha.v.beta.3, cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT 115926-52-8, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Grb-2 and phosphatidylinositol 3-kinase assocn. with IRS-1)
IT 9004-10-8, Insulin, biological studies 9004-10-8D, Insulin, analogs **9004-61-9D, Hyaluronic acid**, conjugates with .alpha.v.beta.3 integrin ligands 9005-25-8D, Starch, conjugates with .alpha.v.beta.3 integrin ligands 9005-49-6D, Heparin, conjugates with .alpha.v.beta.3 integrin ligands 9007-28-7D, Chondroitin sulfate, conjugates with .alpha.v.beta.3 integrin ligands 9050-30-0D, Heparan sulfate, conjugates with .alpha.v.beta.3 integrin ligands 26009-03-0D, Polyglycolic acid, conjugates with .alpha.v.beta.3 integrin ligands 26023-30-3D, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)], conjugates with .alpha.v.beta.3 integrin ligands 26100-51-6D, Polylactic acid, conjugates with .alpha.v.beta.3 integrin ligands 26124-68-5D, Polyglycolic acid, conjugates with .alpha.v.beta.3 integrin ligands 61912-98-9, Insulin-like growth factor 61912-98-9D, Insulin-like growth factor, analogs 133656-20-9D, **hyaluronic acid** conjugates
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)
IT 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effect of ligand binding of .alpha.v.beta.3 integrin on DNA synthesis in EGF-stimulated Rat-1 fibroblasts)
IT 99896-85-2 120103-84-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptide with sequence of; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

IT 133656-20-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.v.beta.3 integrin ligand; cooperative combination of .alpha.v.beta.3 integrin ligand and second ligand contained within a matrix, and use in wound healing and tissue regeneration)

L106 ANSWER 8 OF 11 CA COPYRIGHT 2000 ACS
AN 125:1386 CA
TI **Hyaluronic acid** for the treatment of disease and conditions associated with **macrophage** infiltration in particular stroke and myocardial infarction
IN Turley, Eva Anne; Asculai, Samuel Simon
PA Hyal Pharmaceutical Corporation, Can.
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-725
CC **1-8** (Pharmacology)
FAN.CNT 21

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9605845	A2	19960229	WO 1995-CA467	19950802	<--
	WO 9605845	A3	19960411			
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT					
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CA 2130762	AA	19960225	CA 1994-2130762	19940824	<--
	AU 9531070	A1	19960314	AU 1995-31070	19950802	<--
	AU 701014	B2	19990121			
	EP 777487	A1	19970611	EP 1995-926813	19950802	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	HU 76895	A2	19971229	HU 1997-1518	19950802	<--
	JP 10506884	T2	19980707	JP 1995-507669	19950802	<--
	ZA 9507056	A	19960326	ZA 1995-7056	19950823	<--
	CN 1131539	A	19960925	CN 1995-116616	19950823	<--
	AU 9672721	A1	19980515	AU 1996-72721	19961018	<--
	EP 952855	A1	19991103	EP 1996-934250	19961018	<--
	R: DE, FR, GB, IT, SE					

PRAI US 1994-200309 19940223 <--
CA 1994-2130762 19940824 <--
WO 1995-CA467 19950802 <--
WO 1996-CA700 19961018 <--

AB The treatment of a human having a disease or condition characterized by macrophage, neutrophil or other white blood cell infiltration into an area damaged by the disease or condition comprises the use of an effective amt. of **hyaluronic acid** and/or salts thereof for a period of time until such use is no longer required. Combined use of **hyaluronic acid** and a NSAID, an anti-stroke drug, clot-dissolving drug, a .beta.-blocker, aspirin, streptokinase, and anti-**platelet** drugs (heparin or plasminogen activator) is also claimed.

ST **hyaluronate** macrophage infiltration stroke infarct

IT Blood **platelet** aggregation inhibitors
Thrombolytics
(**hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)

IT Leukocyte
Macrophage
Neutrophil

(infiltration; **hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT Heart, disease
(infarction, **hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT Inflammation inhibitors
(nonsteroidal, **hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT Brain, disease
(stroke, **hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT Adrenergic antagonists
(.beta.-, **hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT **9004-61-9, Hyaluronic acid 9067-32-7**
, Sodium hyaluronate
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(**hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)
IT 50-78-2, Aspirin 9002-01-1, Streptokinase 9005-49-6, Heparin, biological studies 105913-11-9, Plasminogen activator
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hyaluronic acid** for treatment of diseases assocd. with macrophage infiltration)

L106 ANSWER 9 OF 11 CA COPYRIGHT 2000 ACS
AN 123:74854 CA
TI Single dose **toxicity** study of a 1 per cent solution of **sodium hyaluronate** (SI-4402) in rats
AU Toyoshi, Tohru; Isowa, Koichi; Nakajima, Takehiro; Mitsuzono, Toji; Takahashi, Toyomi; Miyauchi, Satoshi
CS JBC Inc., Gifu, 503-06, Japan
SO Oyo Yakuri (**1995**), 50(1), 41-5
CODEN: OYYAA2; ISSN: 0300-8533
DT Journal
LA Japanese
CC **1-12** (Pharmacology)
AB SI-4402 is a 1 per cent soln. of **sodium hyaluronate** (Na-HA) in phosphate-buffered physiol. saline. This soln. is a newly developed ophthalmo-surgical aid for the anterior segment surgery. Acute oral, s.c. and i.p. toxicity tests were made of SI-4402 in Sprague-Dawley rats of both sexes. The results were as follows: no death occurred in any animals by any administration route although the highest doses tech. possible were administered. The oral, s.c. and i.p. LD50 values of SI-4402 were estd. to exceed 50 mL/kg (500 mg Na-HA/kg), 200 mL/kg (2,000 mg Na-HA/kg) and 200 mL/kg (2,000 mg Na-HA/kg), resp. Oral administration of SI-4402 had no effects on general appearance, body wt. or necropsy findings. No toxic signs were obsd. in animals administered SI-4402 s.c. or i.p., except for skin protuberance and abdominal distention, resp., which were considered to be due to the retention of unabsorbed test material. In animals given SI-4402 by these routes, an increase of body wt. caused by unabsorbed test material was obsd. and a retention of test material in the injection site was recognized at the terminal necropsy. In animals administered SI-4402 s.c., histopathol. examn. revealed granulation tissue formation and appearance of macrophages in the subcutis, which were considered to be biol. reactions to the unabsorbed test material. In addn., one female showed dermal ulcer and necrosis with inflammatory cell infiltration in the subcutis of injection site and splenic extramedullary **hematopoiesis**. Since SI-4402 induced no toxic changes when administered orally, s.c. or i.p. to Sprague-Dawley rats of either sex at the highest possible doses, it is concluded that the toxicity of SI-4402 is extremely low.
ST **sodium hyaluronate** SI 4402 toxicity
IT **9067-32-7, Sodium hyaluronate**
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic**

use); BIOL (Biological study); **USES (Uses)**
(single dose toxicity study of a 1 per cent soln. of **sodium hyaluronate** (SI-4402) in rats)

L106 ANSWER 10 OF 11 CA COPYRIGHT 2000 ACS
AN 121:246185 CA
TI **Hyaluronic acid** inhibits polycation-induced cellular **responses**
AU Ialenti, A.; Ianaro, A.; Brignola, G.; Marotta, P.; Rosa, M. Di
CS Department of Experimental Pharmacology, University of Naples 'Federico II', Naples, 49-80131, Italy
SO Mediators Inflammation (**1994**), 3(4), 287-9
CODEN: MNFLEF; ISSN: 0962-9351
DT Journal
LA English
CC **1-12** (Pharmacology)
AB Pos. charged macromols. cause a variety of pathol. events through their electrostatic interaction with anionic sites present on the membrane of target cells. The present study investigated the effect of **hyaluronic acid**, a neg. charged mol., on rat paw edema induced by poly-L-lysine as well as on the histamine release from rat **mast cells** and NO formation by rabbit aorta, both induced by this polycation. **Hyaluronic acid** suppressed these poly-L-lysine-induced effects, possibly due to its neg. charges, which may balance the effects of pos. charged polycations.
ST polycation pathol effect **hyaluronate**; polylysine pathol effect **hyaluronate**
IT Antihistaminics
Inflammation inhibitors
(**hyaluronic acid** as)
IT **Mast cell**
(**hyaluronic acid** suppression of histamine release by **mast cell**)
IT Artery
(aorta, **hyaluronic acid** suppression of nitric oxide formation by aorta)
IT Cations
(polyvalent, **hyaluronic acid** inhibition of cellular responses to)
IT 25104-18-1, Poly-L-lysine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**hyaluronic acid** inhibition of cellular responses to)
IT **9004-61-9, Hyaluronic acid**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(**hyaluronic acid** inhibition of cellular responses to polycations)
IT 51-45-6, Histamine, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**hyaluronic acid** suppression of histamine release by **mast cell**)
IT 10102-43-9, Nitric oxide, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**hyaluronic acid** suppression of nitric oxide formation by aorta)

L106 ANSWER 11 OF 11 CA COPYRIGHT 2000 ACS
AN 120:95787 CA
TI Use of **exogenous** glycosaminoglycans or derivatives in the treatment of thrombopenias
IN Han, Zhong Chao; Caen, Jacques; Lormeau, Jean Claude; Petitou, Maurice
PA Elf Sanofi, Fr.; Institut des Vaisseaux et du Sang
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT **Patent**

LA French
IC ICM A61K031-725
ICS A61K031-73; A61K031-795; A61K031-70
CC **1-8** (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9323059	A1	19931125	WO 1993-FR458	19930511 <--
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2691066	A1	19931119	FR 1992-5949	19920515 <--
	FR 2691066	B1	19950609		
	EP 641213	A1	19950308	EP 1993-910111	19930511 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07506584	T2	19950720	JP 1993-519938	19930511 <--
PRAI	FR 1992-5949	19920515 <--			
	WO 1993-FR458	19930511 <--			

AB **Exogenous** glycosaminoglycans, their analogs, fractions, fragments, and derivs. are used in the prepn. of drugs for the treatment of thrombopenias. The glycosaminoglycans include heparin, heparan sulfate, dermatan sulfate, **hyaluronic acid**, etc. Thus, megakaryocytopoiesis (i.e. CFU-MK formation) was stimulated by e.g. heparan sulfate.
ST glycosaminoglycan thrombopenia; megakaryocytopoiesis glycosaminoglycan; heparin thrombopenia; heparan sulfate thrombopenia; dermatan sulfate thrombopenia; **hyaluronic acid** thrombopenia
IT Glycosaminoglycans, biological studies
RL: BIOL (Biological study)
(for thrombopenia treatment)
IT Anticoagulants and Antithrombotics
(glycosaminoglycans or derivs. without activity of, for thrombopenia treatment)
IT **Hematopoiesis**
(of CFU-MK, glycosaminoglycans stimulation of, thrombopenia treatment in relation to)
IT Blood **platelet**
(disease, thrombocytopenia, treatment of, glycosaminoglycans for)
IT **Hematopoiesis**
(megakaryocytopoiesis, glycosaminoglycans stimulation of, thrombopenia treatment in relation to)
IT **Hematopoiesis**
(thrombocytopoiesis, Fraxiparin stimulation of, thrombopenia treatment in relation to)
IT 96-82-2D, esters with sulfuric acid **9004-61-9**, **Hyaluronic acid 9004-61-9D**, **Hyaluronic acid**, derivs. 9005-49-6, Heparin, biological studies 9005-49-6D, Heparin, derivs. 9042-14-2, Dextran sulfate 9049-31-4, Alginic acid sulfate 9050-30-0, Heparan sulfate 9050-30-0D, Heparan sulfate, derivs. 24967-93-9 24967-93-9D, derivs. 24967-94-0, Dermatan sulfate 24967-94-0D, Dermatan sulfate, derivs. 25191-25-7, Polyvinyl sulfate 25322-46-7 25322-46-7D, derivs. 37300-21-3, Pentosan polysulfate 54182-58-0, Sucralfate
RL: BIOL (Biological study)
(for thrombopenia treatment)

=> fil wpids
FILE 'WPIDS' ENTERED AT 08:55:35 ON 08 APR 2000

FILE LAST UPDATED: 06 APR 2000 <20000406/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK 200017 <200017/DW>
DERWENT WEEK FOR CHEMICAL CODING: 200017
DERWENT WEEK FOR POLYMER INDEXING: 200017
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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    SEE http://www.derwent.com/covcodes.html  <<<

=> d his l107-

     (FILE 'CA' ENTERED AT 08:41:54 ON 08 APR 2000)

     FILE 'WPIDS' ENTERED AT 08:42:23 ON 08 APR 2000
L107       1473 S L6
L108        720 S R03231/DCN OR R06437/DCN
                E SODIUM HYALURON/DCN
                E E4+ALL/DCN
L109         75 S E2
L110       1706 S L107-L109
                E PILARSKI L/AU
L111          3 S E3,E4
L112          1 S L110 AND L111
L113        131 S L110 AND (B14-D02 OR B14-F04 OR B14-G01 OR B14-G02A OR B14-G0
L114          4 S L110 AND (C14-D02 OR C14-F04 OR C14-G01 OR C14-G02A OR C14-G0
L115         84 S L110 AND (B12-G01A OR B12-H01 OR B12-A01 OR B12-A06 OR B12-D0
L116         12 S L110 AND (C12-G01A OR C12-H01 OR C12-A01 OR C12-A06 OR C12-D0
L117        283 SEA L110 AND (P420 OR P431 OR P433 OR P631 OR P633 OR P714)/M0,
                M1,M2,M3,M4,M4,M5
L118        360 S L113-L117
L119         10 S L118 AND (HEMATOPOIE? OR HAEMATOPOIE? OR DENDRITIC OR ERYTHRO
L120         10 S L112,L119

     FILE 'WPIDS' ENTERED AT 08:55:35 ON 08 APR 2000

=> d all abeq tech tot l120

L120 ANSWER 1 OF 10  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
AN   2000-072391 [06]    WPIDS                                          X
DNN  N2000-056661        DNC C2000-020647
TI   A kit for preparing a composite bone graft.
DC   B04 D22 P32
IN   MUSCHLER, G F
PA   (CLEV-N) CLEVELAND CLINIC FOUND
CYC  21
PI   WO 9959500    A2 19991125 (200006)* EN   23p    A61F000-00
        RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
         W: AU CA JP
ADT  WO 9959500 A2 WO 1999-US11413 19990521
PRAI US 1998-82984    19980521
IC   ICM  A61F000-00
AB   WO   9959500 A UPAB: 20000203
     NOVELTY - A kit (A) for preparing a composite bone graft from a bone
     marrow aspirate suspension comprises a porous, biocompatible, implantable
     substrate; and a container to hold the substrate. The container is
     configured to permit the flow of the bone marrow aspirate suspension. The
     container has an inner surface and two ends, each of the ends defining an
     opening.
          DETAILED DESCRIPTION - The kit further comprises a fluid flow
     regulator attachable to one end of the container for regulating the rate
     of flow of the bone marrow aspirate suspension through the substrate. The
     kit also has a reservoir  to hold the bone marrow aspirate suspension and
     a fluid flow regulator attachable to the reservoir for regulating flow of
     the bone marrow aspirate suspension from the reservoir into said
```

container. The kit has an effluent receiver for receiving an effluent of the bone marrow aspirate suspension from the container. The substrate, which is sterile, has external dimensions and a total accessible surface area at least five times greater than the surface area of a solid object having the same external dimensions. INDEPENDENT CLAIMS are also included for the following:

(1) A kit for preparing an implantable graft having platelets attached to the surface.

(2) A composite bone marrow graft.

USE - For preparation of bone grafts.

ADVANTAGE - The bone graft preparation has an enriched population of connective tissue **progenitor cells** and a greater number of **progenitor cells** per unit volume that is found in the original bone marrow aspirate.

DESCRIPTION OF DRAWING(S) - Figure of a schematic representation of the composite bone graft apparatus.

Dwg.1/5

FS CPI GMPI

FA AB; GI; DCN

MC CPI: B04-B04E; B04-C02; B04-N02; B05-B02A3; B11-C04; **B14-N01**; D09-C01D

TECH UPTX: 20000203

TECHNOLOGY FOCUS - BIOTECHNOLOGY - The substrate is formed from a ceramic comprising calcium phosphate or bioglass. The substrate is formed from a material selected from collagen, mineralized bone and demineralized bone. The substrate is formed from **hyaluronic acid** or a synthetic biopolymer. The substrate comprises cell adhesion molecules and growth factors bound to the its surface. The substrate comprises antibodies that bind to surface antigens expressed on the surface of connective tissue **progenitor cells** or platelets. The antibodies are bound to the accessible surface of the substrate. The substrate has pores or passageways having a diameter greater than 40 mum. The container comprises a porous member for retaining the substrate within the container. The container is made of a material that is biocompatible. The substrate is formed from a synthetic biopolymer or **hyaluronic acid**. The substrate has external dimensions and a total accessible surface area at least five times greater than the surface area of a solid object having the same external dimensions.

L120 ANSWER 2 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1999-550865 [46] WPIDS

DNN N1999-407626 DNC C1999-160646

TI Preparation of a living chimeric skin replacement.

DC A25 A96 B04 D16 D22 P34

IN MANSBRIDGE, J N; NAUGHTON, G K; PINNEY, R E

PA (ADTI-N) ADVANCED TISSUE SCI INC

CYC 83

PI WO 9943787 A2 19990902 (199946)* EN 25p C12N005-06

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

AU 9933077 A 19990915 (200004) C12N005-06

ADT WO 9943787 A2 WO 1999-US3859 19990223; AU 9933077 A AU 1999-33077 19990223

FDT AU 9933077 A Based on WO 9943787

PRAI US 1998-75704 19980224

IC ICM C12N005-06

ICS A61K035-36; A61L027-00; C12N005-08; C12N005-10

AB WO 9943787 A UPAB: 19991110

NOVELTY - A living chimeric skin replacement, is new.

DETAILED DESCRIPTION - The preparation of a living chimeric skin replacement comprises:

(a) harvesting autologous epithelial cells from a patient; and

(b) seeding them onto a biocompatible substrate containing allogeneic

epithelial cells cultured in vitro.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for making a chimeric skin replacement comprises the preparation process above;

(2) a method for implanting a chimeric skin replacement at a wound site, comprising:

(a) harvesting autologous epithelial cells from a patient; and either

(b) seeding the autologous cells onto a biocompatible substrate containing allogenic epithelial cells cultured in vitro to form a chimeric skin replacement and implanting the living chimeric skin replacement at the wound site by inverting the chimeric skin replacement so that the cells face into the wound site; or

(c) seeding the autologous epithelial cells into the wound site and implanting a biocompatible substrate containing allogeneic epithelial cells cultured in vitro into the wound site by inverting the substrate so that the allogeneic cells face inward toward the autologous cells;

(3) a composite skin replacement, having an inner, middle and outer component, comprising:

(a) an inner component comprising a biocompatible dermal construct having a biodegradable or removable scaffold as a base;

(b) a middle component comprising epithelial cells; and

(c) an outer component comprising epithelial cells cultured in vitro on a dermal construct comprising a dermal portion having a biodegradable or removable scaffold as a base, the dermal portion being combined with a transitional covering and facing inward toward the middle component of epithelial cells;

(4) a method of implanting a composite skin replacement of (3) into a wound site;

(5) a method for making a composite skin replacement in vivo at a wound site comprising:

(a) implanting an inner biocompatible first dermal construct having a biodegradable or removable scaffold as a base into the wound site;

(b) harvesting autologous epithelial cells from a patient;

(c) seeding the autologous epithelial cells on top of the inner dermal construct in the wound site; and

(d) implanting, on top of the autologous cells, an outer second dermal construct having epithelial cells cultured in vitro and comprising a dermal portion having a biodegradable or removable scaffold as a base, in combination with a transitional covering, so that the epithelial cells of the outer dermal construct face into the wound site; and

(6) a method for making a composite skin replacement in vitro, comprising:

(a) seeding epithelial cells on a first biocompatible dermal construct having a biodegradable or removable scaffold as a base; and

(b) placing a second dermal construct having epithelial cells cultured thereon and comprising a dermal portion having a biodegradable or removable scaffold as a base, in combination with a transitional covering, onto the first dermal construct, such that the cells of the second dermal construct face the cells on the first dermal construct.

ACTIVITY - Vulnerary.

MECHANISM OF ACTION - None given.

USE - The chimeric skin replacement is used where the wound site is a deep or full thickness wound, such as with burns.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V02; B04-C02E; B04-F0200E; B04-H19; B04-H20A; B04-N02; **B14-G02C**; B14-N17B; D05-H02; D05-H08; D05-H14B2; D05-H18; D09-C01; D09-C04B

TECH UPTX: 19991110

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred materials: The allogenic cells comprise keratinocytes and/or melanocytes. The allogenic cells are confluent, especially 25-90% confluent. The allogenic cells are genetically engineered cells. The autologous cells comprise keratinocytes and/or melanocytes. The substrate is biodegradable. The substrate is a synthetic hydrophilic polyarethane membrane, a **hyaluronic**

acid membrane, a fibronectin mat, a fibrin glue, a collagen gel, or a hydrogel. The autologous cells are seeded at a density of about 1x10 to the power of 4/cm2. The ratio of autologous cells to allogenic cells is in the range of 1:5 to 1:50. The biocompatible substrate containing allogenic cells cultured in vitro has been cryopreserved and thawed prior to seeding with autologous cells. The dermal construct of the inner component comprises mesenchymal **stem cells**. The epithelial cells of the outer component are cultured in vitro on the dermal portion of the construct. The transitional covering of the outer component is a membrane. The membrane is a sialastic membrane. The epithelial cells of the outer component are autologous and/or allogenic. The outer component has been further modified by the addition of autologous and/or allogenic proteins. The epithelial cells of the middle component are in the form of sheets, single cell suspensions, microskin bits, or disrupted or dispersed skin. The epithelial cells of the middle component are autologous and/or allogenic. The epithelial cells are keratinocytes and/or melanocytes. The epithelial cells are genetically engineered.

Preferred methods: (2) further comprises implanting a dermal replacement into the wound site prior to implanting the chimeric skin replacement, the chimeric skin replacement being inserted so that the cells of the chimeric skin replacement face inward toward the dermal replacement.

L120 ANSWER 3 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-609979 [51] WPIDS
DNC C1998-182811
TI New block or graft co-polymers for use in coatings - comprise poly-cationic block and at least one non-tissue binding block.
DC A96 B04 D22 G02
IN ELBERT, D L; HERBERT, C B; HUBBELL, J A
PA (CALY) CALIFORNIA INST OF TECHNOLOGY
CYC 73
PI WO 9847948 A1 19981029 (199851)* EN 54p C08G081-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AU BA BB BG BR CA CN CU CZ EE GE GW HU ID IL IS JP KP KR LC LK LR LT MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU
AU 9871211 A 19981113 (199913) C08G081-00
EP 975691 A1 20000202 (200011) EN C08G081-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9847948 A1 WO 1998-US7590 19980417; AU 9871211 A AU 1998-71211 19980417; EP 975691 A1 EP 1998-918250 19980417, WO 1998-US7590 19980417
FDT AU 9871211 A Based on WO 9847948; EP 975691 A1 Based on WO 9847948
PRAI US 1997-44726 19970418
IC ICM C08G081-00
ICS A61K009-50
AB WO 9847948 A UPAB: 19990113
Novel block or graft copolymers (A) comprise a polycationic block (I) and at least one non-tissue binding block (II). (I) is linear with molecular weight (mol.wt.) at least 100 kDa or is a **dendritic** (I) with a mol.wt. high enough to provide at least 8 cationic charges. Also claimed is a polymeric coating (A') on a macroscopic surface comprising layers of polycationic and polyanionic (III) materials.

USE - (A) are biocompatible polymers which can be applied to biological or other surfaces to minimise cell-cell interactions and adhesion of cells or tissues to the surfaces. They are used to encapsulate, plug, seal or support a macroscopic surface. Coatings of (A) or coatings (A') are used to prevent or minimise tissue adhesion and post-operative adhesion; prevent thrombosis; prevent implantation of cancerous cells; coat tissue to encourage healing or prevent infection; enhance local delivery of bioactive agents; or coat metal medical implants (all claimed). The coatings are especially applied to the surfacers of tissues or medical devices, and may incorporate drugs or other biologically active agents.

ADVANTAGE - (A) are biocompatible and resistant to degradation for a specific time period, and can be applied to living cells and tissues in a

very short time period, e.g. during operations.
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: A12-M; A12-V01; A12-V03; B04-C02; B04-C03B; B04-C03C; B11-C04A; B11-C05; B12-M11E; B14-A01; **B14-F04**; **B14-H01**; D09-C05; G02-A05; G04-B02

L120 ANSWER 4 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-512243 [47] WPIDS
DNC C1997-163414
TI Use of **hyaluronic acid** and salts - for treating e.g. immunosuppression, anaemia, osteoporosis, cancer, allergy, asthma, transplantation(s) or auto-immune-like conditions.
DC B04 D16
IN **PILARSKI, L M**
PA (HYAL-N) HYAL PHARM CORP
CYC 77
PI WO 9733592 A1 19970918 (199747)* EN 63p A61K031-725
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
ZA 9702124 A 19971126 (199802) 71p C07D000-00
AU 9720888 A 19971001 (199805) A61K031-725
CA 2173272 A 19971003 (199817) A61K031-725
CA 2199756 A 19970914 (199916) A61K031-725
EP 914133 A1 19990512 (199923) EN A61K031-725
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9733592 A1 WO 1997-CA172 19970312; ZA 9702124 A ZA 1997-2124 19970312; AU 9720888 A AU 1997-20888 19970312; CA 2173272 A CA 1996-2173272 19960402; CA 2199756 A CA 1997-2199756 19970312; EP 914133 A1 EP 1997-906061 19970312, WO 1997-CA172 19970312
FDT AU 9720888 A Based on WO 9733592; EP 914133 A1 Based on WO 9733592
PRAI CA 1996-2173272 19960402; US 1996-13401 19960314
REP 1.Jnl.Ref; US 4725585; WO 9605845
IC ICM A61K031-725; C07D000-00
ICS C07H000-00
AB WO 9733592 A UPAB: 19971125
Use of forms of **hyaluronic acid** (HA) having a mol. wt. < 750 kDa, selected from HA and salts for:
(1) the same purposes known for using recombinant granulocyte-macrophage colony stimulating factor (GM-CSF) or granulocyte-colony stimulating factor (G-CSF);
(2) the same purposes known for using recombinant erythropoietin (EPO);
(3) stimulating the production/release of **haematopoietic** cells and **dendritic**-type cells from the bone marrow and other tissues into the blood;
(4) stimulating and activating stromal cells;
(5) releasing cancer cells from the bone marrow and other tissues into the blood;
(6) mobilising **haematopoietic** cells from the bone marrow and other tissues in a human into the blood of the human;
(7) generating **stem cells** for transplantation;
(8) treating immunosuppression caused by chemotherapy;
(9) treating immunosuppression in a patient caused by AIDS;
(10) treating cancer;
(11) increasing the level of red cells in the blood;
(12) mobilising any type of susceptible cells from one tissue to another, as a single agent or before/during clinical procedures as taught for **haematopoietic** and other types of normal or malignant cells;
(13) mobilising **haematopoietic** cells before and during harvesting of tissue to be used for organ transplantations;
(14) mobilising **haematopoietic** and **dendritic**-type

cells out of an ex vivo organ that has already been harvested from the donor;

(15) treating host individuals about to receive an organ transplant prior to and during the transplantation procedure;

(16) mobilising **haematopoietic** cells and **dendritic** -type cells away from/out of an organ graft that shows signs of immunologic rejection;

(17) optimising the immunosuppressive regimens used in patients to dampen or inhibit immune responses, and

(18) maximising chemotherapeutic kill of **haematopoietic** and **dendritic**-type cells in patients benefiting from same, are new.

USE - The HA and salts can be used, e.g. for treating immunosuppression, anaemia, osteoporosis, treating cancer, treating allergy and asthma, performing organ transplantation, performing **haematopoietic** cell transplantation, treating organ/tissue rejection, treating autoimmune-like conditions, and for in vitro fertilisation and in vivo fertility treatments.

The dosage of HA is at least 1-5 (especially at least 1.5)mg/kg body weight. Ha is applied in two dosages a priming dosage and an additional dosage (claimed).

ADVANTAGE - The HA has fewer side effects than the cytokines GM-CSF, G-CSF and EPO and also acts more rapidly.

Dwg.0/6

FS CPI
FA AB; DCN
MC CPI: B04-C02E; **B14-D02**; B14-F03; **B14-G01**; **B14-G02A**; **B14-G02C**; B14-G02D; **B14-H01**; **B14-K01A**; **B14-N01**; D05-H

L120 ANSWER 5 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-489242 [45] WPIDS
DNC C1997-155843
TI Increasing or decreasing transfection efficiency - by altering amount of membrane-associated proteoglycans and optionally plasma concentrations of glycosaminoglycans.
DC B04 D16
IN MISLICK, K A
PA (CALY) CALIFORNIA INST OF TECHNOLOGY
CYC 76
PI WO 9734483 A1 19970925 (199745)* EN 64p A01N043-04
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN YU
AU 9722145 A 19971010 (199806) A01N043-04
US 5783566 A 19980721 (199836) A61K038-00
ADT WO 9734483 A1 WO 1997-US4217 19970312; AU 9722145 A AU 1997-22145 19970312; US 5783566 A US 1996-644095 19960510
FDT AU 9722145 A Based on WO 9734483
PRAI US 1996-644095 19960510; US 1996-13647 19960318
REP 3.Jnl.Ref; US 5459127
IC ICM A01N043-04; A61K038-00
ICS A61K009-127; A61K031-70; A61K031-725; A61K038-16; A61K048-00; C07J009-00; C07K001-00; C07K014-00; C07K017-00; C12N005-00; C12N015-00
AB WO 9734483 A UPAB: 19971113
Methods to increase the administration of genetic material to cells in vitro, in vivo or ex vivo, comprises administering to the cells an effective amount of a complex of genetic material and a cationic species, and an effective amount of a compound that increases proteoglycan expression on the cell surface, to increase the transfection efficiency relative to when the cells exhibit normal proteoglycan expression, and

Also claimed are:

(1) a method to decrease the administration of genetic material to cells in vitro, in vivo or ex vivo comprising administering to the cells a

compound that reduces the expression of proteoglycans on the cell surface to decrease the efficiency of adminstration of complexes of genetic material and cationic species to the cell, where the compound is chosen from protease inhibitors, plasma lipoproteins, growth factors, lipolytic enzymes, extracellular matrix proteins, platelet factors 4, interleukin 4 (IL-4) alpha -and beta , and TNF- alpha , and

(2) an improved lipid for mediating transfection, comprising a cationic lipid, a neutral phospholipid, a lyso-lipid, or a neutral lipid that includes a side chain selected from phorbol esters or anabolic, catabolic and modulating cytokines.

USE - The method can be used to transfect liver cells, with the low density lipoprotein (LDL) receptor to reduce serum cholesterol in vivo, or to treat **progenitor cells** from the **haematopoietic** system at a pre-differential stage to correct hereditary disorders.

The method can be used to treat cells to express interferon (IFN) and cytokines to stimulate the immune system to react against foreign antigens or cancers or to make cancer cell more chemosensitive (all claimed).

ADVANTAGE - By increasing the amount of membrane-associated proteoglycans in the cell, and optionally decreasing the plasma concentration of glycosaminoglycans, the transfection efficiency can be increased. By decreasing the amount of membrane-associated proteoglycans in the cell, and optionally decreasing the plasma concentration of glycosaminoglycans, the transfection efficiency can be decreased. Transfection efficiency can be controlled, whether preformed in vivo, ex vivo or in vitro.

Dwg.3B/5

FS CPI
FA AB; GI; DCN
MC CPI: B04-H02D; B04-H06; B04-H06B; B04-H08; B04-L01; B04-M01; B04-N04; B04-N05; D05-H08; D05-H18

L120 ANSWER 6 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-297882 [27] WPIDS
DNN N1997-246163 DNC C1997-096572
TI Material comprising extracellular matrix from specific connective tissue cells - and three-dimensional matrix of **hyaluronic acid** derivative, for treating injuries to cartilage, bone and skin, and used as substrate for in vitro growth of keratinocytes.
DC B04 D16 D22 P34
IN ABATANGELO, G; CALLEGARO, L
PA (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
CYC 75
PI WO 9718842 A1 19970529 (199727)* EN 35p A61L027-00
RW: AT BE CH DE DK ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9676934 A 19970611 (199740) A61L027-00
EP 863776 A1 19980916 (199841) EN A61L027-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT RO SE SI
IT 1282207 B 19980316 (199938) A61K000-00
AU 709236 B 19990826 (199946) A61L027-00
JP 2000500372 W 20000118 (200014) 32p A61L027-00
ADT WO 9718842 A1 WO 1996-EP5093 19961119; AU 9676934 A AU 1996-76934 19961119; EP 863776 A1 EP 1996-939845 19961119, WO 1996-EP5093 19961119; IT 1282207 B IT 1995-PD225 19951120; AU 709236 B AU 1996-76934 19961119; JP 2000500372 W WO 1996-EP5093 19961119, JP 1997-519385 19961119
FDT AU 9676934 A Based on WO 9718842; EP 863776 A1 Based on WO 9718842; AU 709236 B Previous Publ. AU 9676934, Based on WO 9718842; JP 2000500372 W Based on WO 9718842
PRAI IT 1995-PD225 19951120
REP 1.Jnl.Ref; EP 265116; EP 462426; EP 526865; US 5197985; US 5520916; WO 9311803; WO 9637519
IC ICM A61K000-00; A61L027-00

ICS A61L015-28; C12N005-00; C12N005-06
AB WO 9718842 A UPAB: 19970702
Biological material (A) comprises:
(a) culture of autologous or homologous bone marrow **stem cells** (SC), (partially) differentiated into cell lines of a specific connective tissue and the extracellular matrix (ECM) produced by these connective tissue cells, and
(b) a 3-dimensional, biocompatible and biodegradable matrix (M) made of **hyaluronic acid** (HA) derivative (I).
Alternatively, (a) is replaced by (a1) cell-free ECM secreted by either (partially) differentiated SC or the specified mature connective tissue cells.
USE - (A) are used:
(i) for covering areas of eroded or degraded cartilage (ECM then produced by chondrocytes);
(ii) in cases of loss of bone material (osteoblasts);
(iii) as in vitro substrates for seeding with keratinocytes for subsequent grafting (fibroblasts), or
(iv) as skin substitutes for dressing wounds (fibroblasts) (all claimed).
ADVANTAGE - Autologous cells in (A) remain in newly formed connective tissue and contribute towards wound repair by secreting growth factors and ECM.
If only homologous cells are available, then use of (a1) in place of (a) avoids adverse immunological reactions.
(A) can be frozen to produce a tissue bank.
Dwg.0/5
FS CPI GMPI
FA AB; DCN
MC CPI: B04-F07; B14-N17B; D05-H08; D05-H10; D09-C01D

L120 ANSWER 7 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-244730 [22] WPIDS
DNC C1997-079226
TI Sustained release of granulocyte-macrophage colony stimulating factor - from biodegradable microparticles or hydrogels, useful for stimulating **haematopoietic** cell proliferation and as vaccine adjuvant.
DC A96 B04 B07
IN GOMBOTZ, W; HUANG, W J; LAWTER, J R; PANKEY, S; PETTIT, D; LAWTER, J
PA (AMCY) AMERICAN CYANAMID CO; (IMMV) IMMUNEX CORP
CYC 23
PI WO 9713502 A2 19970417 (199722)* EN 49p A61K009-16
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NZ
AU 9674384 A 19970430 (199734) A61K009-16
WO 9713502 A3 19971002 (199814) A61K009-16
EP 859601 A2 19980826 (199838) EN A61K009-16
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5942253 A 19990824 (199941) — A61K009-50
JP 11513667 W 19991124 (200006) 52p A61K038-22
AU 714074 B 19991216 (200010) A61K009-16
AU 9954017 A 19991223 (200011) A61K009-16
ADT WO 9713502 A2 WO 1996-US16277 19961010; AU 9674384 A AU 1996-74384 19961010; WO 9713502 A3 WO 1996-US16277 19961010; EP 859601 A2 EP 1996-936356 19961010, WO 1996-US16277 19961010; US 5942253 A US 1995-542445 19951012; JP 11513667 W WO 1996-US16277 19961010, JP 1997-515216 19961010; AU 714074 B AU 1996-74384 19961010; AU 9954017 A Div ex AU 1996-74384 19961010, AU 1999-54017 19991014
FDT AU 9674384 A Based on WO 9713502; EP 859601 A2 Based on WO 9713502; JP 11513667 W Based on WO 9713502; AU 714074 B Previous Publ. AU 9674384, Based on WO 9713502; AU 9954017 A Div ex AU 714074
PRAI US 1995-542445 19951012
REP No-SR.Pub; DE 4406172; US 4897268; WO 9112882; WO 9401133; WO 9506077; WO 9610395
IC ICM A61K009-16; A61K009-50; A61K038-22
ICS A61F002-02; A61K009-14; A61K009-48; A61K031-00; A61K038-18;

A61K038-19; A61K047-34
AB WO 9713502 A UPAB: 19970626
Granulocyte-macrophage colony stimulating factor (I) is administered within biodegradable polymeric microparticles (A) that provide sustained release under physiological conditions. (A) are formed by a process that retains over 60% of the biological activity of (I) after its release from the particle.
Also claimed are:
(1) (A);
(2) microparticles (B) comprising at least 3 polymers (i.e. polylactic, polyglycolic or poly(lactic-glycolic) acids) of different molecular weights (mol. wt.), having dispersed within them a compound to be released;
(3) a formulation for controlled delivery comprising (I) dispersed in a synthetic, polymeric hydrogel which absorbs water up to 90% of the final, hydrated weight, and
(4) combination (C) of (I) with a chemoattractant, biocompatible synthetic polymer.
USE - (I) is used to stimulate proliferation of **haematopoietic** cells (claimed), e.g. in patients prone to infection such as those about to undergo major bowel surgery, trauma victims and those infected with HIV). (I) is used in combination with (C) as an immunostimulant (vaccine adjuvant) (claimed). (A) may be administered orally, topically or by injection, e.g. subcutaneously when using the hydrogel. Typically the dose is 125 mu g/m2/day.
ADVANTAGE - The formulations provide sustained release of (I) over at least 1 week, and the kinetics and manner of release can be controlled by selection of polymer. They require only a single injection, avoiding strong fluctuation in (I) levels associated with multiple injections and possibly reducing the total amount of (I) needed.
Dwg.2c/6
FS CPI
FA AB; GI; DCN
MC CPI: A05-E02; A09-A07; A12-V01; B04-C03D; B04-H04C; B12-M10A; B12-M11E; B14-F02; **B14-G01**; B14-L01

L120 ANSWER 8 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-012192 [02] WPIDS
DNC C1994-005568
TI Antiallergic agents for eye lotions, skin ointments etc. - contain **hyaluronic acid** (salt) for reduced side effects.
DC B04
PA (ELED) DENKI KAGAKU KOGYO KK
CYC 1
PI JP 05320055 A 19931203 (199402)* 4p A61K031-725
ADT JP 05320055 A JP 1991-188279 19910703
PRAI JP 1991-188279 19910703
IC ICM A61K031-725
ICS A61K009-08; A61K009-12
AB JP 05320055 A UPAB: 19940223
Antiallergic agents contain **hyaluronic acid** and/or its non-toxic salts as effective component. The agents are used in the pharmaceutical formulation of nasal drop, eye lotion, skin and membrane ointment, and oral cavity and pharynx propellant.
USE/ADVANTAGE - The agents having new therapeutic actions different from those of the known drugs are useful as antiallergics without side effects in the treatment of bronchial asthma, atopic dermatitis, and pollenosis. **Hyaluronic acid** and its salts can bind to **mast cells** and basophils, thus inhibiting the binding of the cells to immunoglobulins and also preventing the bridging between the cells and immunoglobulin antigens. This leads to the decrease in the liberation of chemical transmitters from the **mast cell**
.
In an example, inhibitions were 62.3% and 34.2% at 0.1% and 0.01% **Na hyaluronate**, respectively, in an in vitro assay of the liberation of histamine from **mast cells** using 1-3

x 10 power 6 cell/ml rat intrapenitreal cells and 10mg/ml rat antioval albumin serum as stimulant. Nasal disorders such as excessive nasal mucus and rhinostegnosis were improved (anaphylaxis inhibition 64.3%) in rats with 20 micron L 0.5% **Na hyaluronate** against 3 mg/ml oval albumin.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-C02; **B14-G02A**; **B14-K01A**; B14-N17C

L120 ANSWER 9 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1993-036102 [04] WPIDS
DNN N1993-027697 DNC C1993-016326
TI Compsn. for stimulating growth of bone or cartilage - contains osteogenic protein, biodegradable porous polymer matrix and sequestrant for the protein, esp. an alkyl cellulose.
DC A96 B04 P32 P73
IN ISAACS, B S; KENLEY, R A; PATEL, H; RON, E; TUREK, T J
PA (GEMY) GENETICS INST INC
CYC 20

PI	WO 9300050	A1	19930107 (199304)*	EN	27p	A61F002-02
	AU 9222542	A	19930125 (199319)			A61F002-02
	FI 9305732	A	19931220 (199410)			A61L000-00
	NO 9304573	A	19931213 (199412)			A61K009-16
	EP 591392	A1	19940413 (199415)	EN		A61F002-02
	JP 06508777	W	19941006 (199444)			A61L027-00
	AU 663328	B	19951005 (199547)			A61K009-00
	EP 591392	B1	19960911 (199641)	EN	11p	A61F002-02
	R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
	DE 69213739	E	19961017 (199647)			A61F002-02
	ES 2094359	T3	19970116 (199710)			A61F002-02
	US 5597897	A	19970128 (199710)		7p	C07K014-51

ADT WO 9300050 A1 WO 1992-US5309 19920622; AU 9222542 A AU 1992-22542 19920622; FI 9305732 A WO 1992-US5309 19920622, FI 1993-5732 19931220; NO 9304573 A WO 1992-US5309 19920622, NO 1993-4573 19931213; EP 591392 A1 EP 1992-914339 19920622, WO 1992-US5309 19920622; JP 06508777 W WO 1992-US5309 19920622, JP 1993-501625 19920622; AU 663328 B AU 1992-22542 19920622; EP 591392 B1 EP 1992-914339 19920622, WO 1992-US5309 19920622; DE 69213739 E DE 1992-613739 19920622, EP 1992-914339 19920622, WO 1992-US5309 19920622; ES 2094359 T3 EP 1992-914339 19920622; US 5597897 A WO 1992-US5309 19920622, US 1993-81378 19930629
FDT AU 9222542 A Based on WO 9300050; EP 591392 A1 Based on WO 9300050; JP 06508777 W Based on WO 9300050; AU 663328 B Previous Publ. AU 9222542, Based on WO 9300050; EP 591392 B1 Based on WO 9300050; DE 69213739 E Based on EP 591392, Based on WO 9300050; ES 2094359 T3 Based on EP 591392; US 5597897 A Based on WO 9300050
PRAI US 1991-718721 19910621; US 1993-81378 19930629
REP US 4637931; US 4917893; EP 145240; US 4563489; WO 8909788; WO 9009783; WO 9200718
IC ICM A61F002-02; A61K009-00; A61K009-16; A61L000-00; A61L027-00; C07K014-51
ICS A61F002-28; A61F002-44; A61K009-14; A61K037-02; A61K037-12; A61K038-39; B32B005-16
AB WO 9300050 A UPAB: 19931119
Compsn. contains an osteogenic protein (I), a polymeric matrix (A) (i.e. homo- or co-polymer of lactic and/or glycolic acids) and, as (I)-sequestering agent, an alkylcellulose (II), **hyaluronic acid**, Na alginate, poly(ethylene glycol), polyoxyethylene, carboxyvinyl polymer or poly(vinyl alcohol).

Also new are (1) particles of (A) of Spherical dia. 150-850 microns and surface area 0.02-4 sq.m/g. and (2) compsn. consisting of (I) and solubilising agent (III).

Pref. (I) is a bone morphogenic protein (esp. BMP-21, transforming growth factor beta, Vgr-1, OP-1, COP-5 and COP-7. (II) is hydroxypropylmethylcellulose or carboxymethylcellulose (CMC), and (A) is esp. a copolymer.

USE/ADVANTAGE - (I) is sequestered in situ by (II) for sufficient time to induce cartilage and/or bone growth when the compsn. is implanted into an injury site, e.g. as a substitute for autologous bone grafts, in treatment of fractures, for bone defect repair etc. The new porous particles permit infiltration by bone **progenitor cells** and their surface area is optimal for inducing bone formation. Being porous they are readily biodegradable and can adsorb proteins. Additionally the particles when formulated with a sequestering agent, can be used as a substitute for bone wax to provide a bioerodible haemosta
Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: A05-E02; A09-A; A12-S09; A12-V01; B04-B04A6; B04-B04J; B04-C02A2; B04-C02D; B04-C02E; B04-C03; B07-D09; B10-A17; B12-H04; **B12-J08**

ABEQ EP 591392 B UPAB: 19961011
A composition comprising a pharmaceutically acceptable admixture of (i) an osteogenic protein; (ii) a polymer matrix component selected from the group consisting of poly(lactic acid), poly(glycolic acid), and copolymers of lactic acid and glycolic acid; and (iii) an osteogenic protein-sequestering alkyl-cellulose or an osteogenic protein-sequestering agent selected from the group consisting of **hyaluronic acid**, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer, and poly(vinyl alcohol).

ABEQ US 5597897 A UPAB: 19970307
A composition comprising a pharmaceutically acceptable admixture of
(i) an osteogenic protein;
(ii) a polymer matrix component selected from the group consisting of poly(lactic acid), poly(glycolic acid), and copolymers of lactic acid and glycolic acid; and
(iii) an osteogenic protein-sequestering alkylcellulose, wherein said alkylcellulose is present in an amount of approximately 0.5-20 wt % based on total composition weight, wherein said osteogenic protein is not encapsulated within the polymer matrix.
Dwg.0/0

L120 ANSWER 10 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-309698 [38] WPIDS
CR 1993-010345 [02]
DNC C1992-137530
TI Compsn. for sustained release of erythropoietin for treatment of anaemia - contains erythropoietin and **hyaluronic acid** in a carrier, diluent or excipient.
DC B04
IN IGARI, Y; OGAWA, Y; YAMADA, M
PA (TAKE) TAKEDA CHEM IND LTD
CYC 3

PI	EP 503583	A1 19920916 (199238)* EN	25p		A61K047-36
	CA 2062659	A 19920913 (199249)			A61K035-14
	CA 2073554	A 19930111 (199313)			A61K047-36
	JP 05065231	A 19930319 (199316)	13p		A61K037-24
	JP 05186362	A 19930727 (199334)	18p		A61K037-02
	US 5416071	A 19950516 (199525)	38p		A61K038-14
	US 5591713	A 19970107 (199708)	36p		A61K037-10

ADT EP 503583 A1 EP 1992-104150 19920311; CA 2062659 A CA 1992-2062659 19920311; CA 2073554 A CA 1992-2073554 19920709; JP 05065231 A JP 1992-52054 19920311; JP 05186362 A JP 1992-182141 19920709; US 5416071 A CIP of US 1992-847188 19920306, US 1992-909160 19920706; US 5591713 A CIP of US 1992-847188 19920306, Div ex US 1992-909160 19920706, US 1995-377392 19950124
FDT US 5591713 A Div ex US 5416071
PRAI JP 1991-170205 19910710; JP 1991-46735 19910312
REP 1.Jnl.Ref; GB 2000213; WO 9005522; WO 9009798; WO 9104058
IC ICM A61K035-14; A61K037-02; A61K037-10; A61K037-24; A61K038-14; A61K047-36
ICS A61K009-08; A61K009-14; A61K027-30; A61K037-00; A61K037-26;

A61K047-42
AB EP 503583 A UPAB: 19950705
Compsn. comprises (a) erythropoietin (EPO), (b) an amt. of **hyaluronic acid** (HA) or its salts effective for the sustained-release of EPO and (c) a carrier, diluent or excipient.
The compsn. may further comprise a water-soluble protein, e.g. human serum albumin (HSA).
USE/ADVANTAGE - When the compsn is administered by injection, the pharmacological efficacy of EPO is sustained over a long time period (not less than 24 hrs.) without interfering with the pharmacological efficacy of the EPO and, at the same time, the abrupt onset of the pharmacological effect of the drug in an early stage after administration is successfully controlled. The compsn. can be used for treating e.g. anaemi
Dwg.0/10
Dwg.0/10
FS CPI
FA AB; DCN
MC CPI: B04-B04A6; B04-B04D2; B04-C02E; **B12-H01**; B12-M10A
ABEQ JP 05186362 A UPAB: 19931119
Water soluble compsns. comprise (a) pharmaceutically active substances or chemically synthetic pharamaceutical active substances which are polypeptides secreted from a living body or their derivs. other than erythropoietin, (b) water-soluble **hyaluronic acid** or its non-toxic salts, and (c) water-soluble protein which shows no pharmacological activity and can be injected into the fluid, are new.
Preferred samples of the polypeptide are cytokines, peptide hormones, growth factors, factor of various kinds which function to the cardiovascular system, central and peripheral neurons, electrolytes and organic substances in the fluid and blood, the bones, respiratory system, gastro-intestinal tract, the immunological system, and genitals.
USE/ADVANTAGE - Compsns. show sustained release activity, and no toxicity caused by the excess concentration of the agents in blood. They can be administered through a thinner needle with reduced pain and reduced contamination of bubbles, because of lower viscosity, compared with conventional compsns. of higher concns. of **hyaluronic acid**.
Dwg.0/0
ABEQ US 5416071 A UPAB: 19950630
Water soluble sustained release pharmaceutical compsn. for injection comprises an admixt. of (i) erythropoietin; (ii) lyaluronic acid or its salt, having mol. wt. 500,000-3,000,000 and (iii) a water soluble protein selected from human serom albumin (HSA), human serum globulin, collagen or gelatin. The wt. ratios of (c) to (b) is 0.001:1 to 100:1, and the wt. ratios of (a) to (b) is 0.0001:1 to 10:1. Pref. the protein is HSA and the compns. is lyophilised.
USE/ADVANTAGE - The compsn. is used to provide sustained release of erythropoietin which acts on erythroblastic **progenitor cells** in bone barrow to promote differentiation into red blood cells. The compsn. can be administered using a small gauge needle and therefore contribuges to relieving pain in patients.
Dwg.0/15
ABEQ US 5591713 A UPAB: 19970220
A water-soluble compsn. comprises (a) a pharmacologically active polypeptide secreted by an animal body or its derivative or a chemically synthesised pharmacologically active substance, (b) a water-soluble species of **hyaluronic acid** or its non-toxic salt and (c) a water-soluble protein injectable into body fluids without showing any substantial pharmacological activity.
Dwg.0/15

=> d his l121-

(FILE 'WPIDS' ENTERED AT 08:42:23 ON 08 APR 2000)

FILE 'WPIDS' ENTERED AT 08:55:35 ON 08 APR 2000

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L121          55 S L118 AND (TRANSPLANT? OR MARROW OR ?ALLERG? OR ?ASTHMA?)
L122          51 S L121 NOT L120
L123          13 S L122 AND (COMBINATION OR RESPIRATORY OR TOPICAL? OR CHITOSAN
L124           5 S L118 AND D05-H/MC
L125          56 SEA L118 AND Q233/M0,M1,M2,M3,M4,M5,M6
L126          54 S L124,L125 NOT L120
L127           1 S L123 AND CONSTRUCT
L128          12 S L123 NOT L127
L129           2 S L126 AND L128
L130          12 S L128,L129
L131          52 S L126 NOT L120,L130
L132          17 S L131 AND (AUGMENT OR GROWTH OR ALLOGRAFT OR MEDICAL USE OR IM
L133          29 S L130,L132

=> d all abeq tech tot l133

L133 ANSWER 1 OF 29  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
AN   2000-195084 [17]   WPIDS
DNN  N2000-144372       DNC C2000-060418
TI   System for reconstructing osseous tissue, useful e.g. for treating
     fractures, comprises scaffold containing promoter of bone
     formation and inhibitor of bone resorption.
DC   A96 B04 D22 P34
IN   BUDNY, J A
PA   (PHAR-N) PHARMACAL BIOTECHNOLOGIES INC
CYC  85
PI   WO 2000004941 A1 20000203 (200017)* EN   43p    A61L027-00
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
         W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
            GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
            LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
            TT UA UG UZ VN YU ZA ZW
ADT  WO 2000004941 A1 WO 1999-US16800 19990722
PRAI US 1998-122348   19980724
IC   ICM  A61L027-00
AB   WO 200004941 A UPAB: 20000405
     NOVELTY - System for reconstitution of osseous tissue comprising a
     scaffold carrying a compound (I) that promotes bone formation and a
     component that decreases bone resorption (II).
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) method for reconstruction of osseous tissue by combining
     components (I) and (II) at a site requiring bone regeneration;
          (2) composition for treating bone tissue comprising a
     scaffold-forming matrix and an adhesion molecule (III) that adheres to
     osteoblasts provided at the treatment site;
          (3) composition for inhibiting proteolysis of extracellular matrix
     (ECM) in bone comprising a biodegradable scaffold-forming matrix with
     attached vitronectin (VN) that is released as the matrix degrades; and
          (4) method for treating bone tissue using the composition of (3) in
     which the matrix (organic and/or inorganic) has a predetermined
     degradation rate.
          ACTIVITY - Bone regenerative; osteopathic.
          MECHANISM OF ACTION - (I) induces migration and adhesion of
     osteoblasts and osteoclasts; (II) inhibits proteolysis (specifically by
     plasmin) of extracellular matrix.
          USE - The system is used to replace, remodel or correct bone defects,
     e.g. fractures, fissures or bone mass loss.
          ADVANTAGE - Incorporation of (I) into the scaffold results in rapid
     seeding by osteoblasts and the development of an organic matrix, i.e. the
     preformed scaffold replaces the rate-determining step of extracellular
     matrix formation. The scaffold can be designed to have a predetermined
     resorption/degradation rate, and may include regulatory compounds for
     specific cell types.
          DESCRIPTION OF DRAWING(S) - The diagram shows the relationship of
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plasmin with its activators and inhibitors.
Dwg.3/3
FS CPI GMPI
FA AB; GI; DCN
MC CPI: A12-V02; B04-C02E; B04-C02E2; B04-C03B; B04-C03C; B04-C03D; B04-N02; **B14-N01**; D05-H10; D09-C01D
TECH UPTX: 20000405
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Systems: The scaffold comprises a polymer that is:
(a) natural (especially collagen, **hyaluronic acid**, heparin, proteoglycan, glycoprotein, lipopolysaccharide, demineralized bone, crosslinked or derivatized natural polymers, materials containing proteoglycans and/or chondroitin sulfate); or
(b) synthetic:
(i) either resorbable (preferably polyester, polyamide and/or homo- or hetero-polymers containing glycolic acid, lactic acid, epsilon-caprolactone and/or other mono- or di-carboxylic acids), optionally including reactive groups for formation of esters or amides; or
(ii) less resorbable (especially polyanhydrides, polyurethanes, polyacrylonitrile, poly(vinyl alcohol), poly(methyl methacrylate) and/or polyphosphazines).
Alternatively the scaffold is inorganic or a mixture of organic and inorganic materials. Component (II) is also a polymeric scaffold attached to a biologically active protein (III).
Preferred Agents: (I) is fibronectin (FN), vitronectin (VN), proteoglycan, collagen, selectin or their fragments; proteins and peptides that facilitate cell adhesion (e.g. RGDC, GRGDSPC, osteonectin, von Willebrand factor, thrombospondin, bone morphogenic proteins); plasminogen activator inhibitor (PAI) or inhibitors of (metallo)proteases. (I) may be attached to the scaffold through a linker, particularly a homo- or hetero-bifunctional crosslinker or a polymer, especially polyethoxylate, poly(ethylene glycol) and/or polysorbitol. (III) is VN, PAI and/or an inhibitor of (metallo)protease and is specifically targeted to receptors (particularly integrins) on osteoblasts. In the composition of (2), (III) is VN or FN, covalently attached to a biodegradable component, particularly an organic polymer that degrades at a controlled rate. In the composition of (3), the matrix also carries at least one of PAI and/or (metallo)protease inhibitor, and in (4) VN is bound to PAI which is released, as the matrix degrades, to inhibit production of proteolytic plasmin.

TECHNOLOGY FOCUS - POLYMERS - Preferred Scaffold Polymers: Suitable polymers for the scaffold are resorbable (specifically polyester, polyamide and/or homo- or hetero-polymers containing glycolic acid, lactic acid, epsilon-caprolactone and/or other mono- or di-carboxylic acids), optionally including reactive groups for formation of esters or amides, or less resorbable (specifically polyanhydrides, polyurethanes, polyacrylonitrile, poly(vinyl alcohol), poly(methyl methacrylate) and/or polyphosphazines. Suitable polymers for linking active proteins to the matrix are polyethoxylate, poly(ethylene glycol) and/or polysorbitol).

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Scaffold: Suitable inorganic materials for the scaffold include mica, silicon dioxide, zeolite, calcite, gypsum etc.

L133 ANSWER 2 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-551207 [46] WPIDS
DNC C1999-160851
TI Inhibition of tumor **growth** and angiogenesis by administration of inhibiting amount of **hyaluronate** binding protein.
DC B04 D16
IN GREEN, S J; UNDERHILL, C B
PA (ENTR-N) ENTREMED INC
CYC 83
PI WO 9945942 A1 19990916 (199946)* EN 52p A61K038-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG UZ VN YU ZW

AU 9930856 A 19990927 (200006) A61K038-00

ADT WO 9945942 A1 WO 1999-US5498 19990312; AU 9930856 A AU 1999-30856 19990312

FDT AU 9930856 A Based on WO 9945942

PRAI US 1998-108124 19981112; US 1998-77898 19980313

IC ICM A61K038-00
ICS A01N037-18; A61K038-04; C07K001-00

AB WO 9945942 A UPAB: 19991110
NOVELTY - A method of inhibiting the growth of a tumor comprises administering to the tumor a growth inhibiting amount of a **hyaluronate** (HA) binding protein, where the protein has an amino acid sequence of at least a portion of a naturally occurring HA binding protein and has a HA binding activity and an anti-tumor activity.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of inhibiting angiogenesis comprises administering to an endothelial cell a growth inhibiting amount of a **hyaluronate** (HA) binding protein, where the protein has an amino acid sequence of at least a portion of a naturally occurring HA binding protein and has a HA binding activity and an anti-angiogenic activity;
(2) an isolated HA binding protein, where the protein has an amino acid sequence of a portion of a naturally occurring HA binding protein and has a HA binding activity and an anti-tumor activity;
(3) a composition comprising a pharmaceutically acceptable excipient and a first HA binding protein as above; and
(4) a nucleic acid coding for a HA binding protein as above.
ACTIVITY - Cytostatic; Anti-angiogenic.
MECHANISM OF ACTION - Tumor Growth Inhibitor.
USE - Metastatin protein inhibits endothelial cell migration in vitro and tumor metastasis in vivo. HA binding proteins, including HA link module peptides, can be labeled isotopically or with other molecules or proteins for use in the detection and visualization of HA binding link module sites. The HA binding proteins also act as agonists and antagonists at the HA binding link module receptor, therefore enhancing or blocking the biological activity of HA binding proteins.
Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: B04-E02F; B04-G01; B04-N02; B12-K04; **B14-H01**; D05-H09; D05-H11; D05-H12A; D05-H17A6

TECH UPTX: 19991110
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Protein: The protein comprises at least a portion of an amino acid sequence of a proteoglycan tandem repeat domain. The protein is metastatin having a molecular weight of approximately 38 kDa as determined by non-reducing gel electrophoresis. The protein comprises at least a portion of a cartilage link protein or an agreggan protein. The protein comprises at least a portion of a naturally occurring HA binding protein chosen from CD44, hyaluronectin, versican, receptor **hyaluronan**-mediated motility (RHAMM), inter-alpha trypsin inhibitor, intracellular **hyaluronan** binding protein (IHABP), I-CAM 1 and TSG-6. The protein is recombinantly expressed, especially in vivo. The protein has an amino acid sequence as follows: QYPITKPREP.
This sequence corresponds to approximately amino acids 216-225 of human cartilage link protein. The protein further has an endothelial cell migration inhibitory activity.

L133 ANSWER 3 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1999-470031 [40] WPIDS

DNC C1999-138087

TI Use of polysaccharides, e.g. **hyaluronic acid**, **chitosan** etc., in cosmetic and dermatological preparations to

provide protection against skin irritations.
DC A11 A96 B07 D21
IN DOERSCHNER, A; ENNEN, J; GOHLA, S; KADEN, W; KIELHOLZ, J; LANZENDOERFER, G; NIELSEN, J; SAUERMANN, G; UNTIEDT, S
PA (BEIE) BEIERSDORF AG
CYC 25
PI DE 19805827 A1 19990819 (199940)* 12p A61K007-48
EP 937454 A2 19990825 (199940) DE A61K007-48
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT DE 19805827 A1 DE 1998-19805827 19980213; EP 937454 A2 EP 1999-102341 19990206
PRAI DE 1998-19805827 19980213
IC ICM A61K007-48
ICS A61K007-40; A61K007-42
AB DE 19805827 A UPAB: 19991004
NOVELTY - Cosmetic and dermatological preparations containing polysaccharides and alpha -hydroxycarboxylic acids, alpha -ketocarboxylic acids and/or amino acids are also new, useful in cosmetic and dermatological preparations to protect sensitive or hypersensitive skin from irritations.
DETAILED DESCRIPTION - Cosmetic and dermatological preparations containing polysaccharides and alpha -hydroxycarboxylic acids, alpha -ketocarboxylic acids and/or amino acids are also new, useful in cosmetic and dermatological preparations to protect sensitive or hypersensitive skin from irritations, especially to prevent stinging.
An INDEPENDENT CLAIM is also included for cosmetic and dermatological preparations containing polysaccharides and alpha -hydroxycarboxylic acids, alpha -ketocarboxylic acids and/or amino acids.
USE - The preparations are used for cosmetic and dermatological skin care, including the treatment or prophylaxis of erythematous, inflammatory, **allergic** and autoimmune-reactive skin conditions. They can also be used to promote wound healing.
ADVANTAGE - The compositions have practically no stinging effects and good skin compatibility.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A03-A00A; A12-V01; A12-V04C; B04-C02E2; B04-C02E3; B14-C03; **B14-G02A**; B14-G02D; B14-N17; B14-N17B; B14-R01; D08-B09A
TECH UPTX: 19991004
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Preparations: Preparations have a polysaccharide content of 0.1-20 wt.%, particularly 1-5 wt.%. Preferred Polysaccharides: The polysaccharide is water-soluble, water-swellable or forms a gel in the presence of water. Especially suitable polysaccharides are **hyaluronic acid**, chitosan and the fucose-rich product FG 1000 (see Chemical Abstracts, Registration Number 178463-23-5).

L133 ANSWER 4 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-243265 [20] WPIDS
DNC C1999-070886
TI **Topical** composition, used in the treatment of pain, inflammation and/or itching - comprises at least one low purity or cosmetic grade complex carbohydrate, and at least one essential oil which can penetrate the dermis of mammals.
DC B04
IN BROWN, H G
PA (DERM-N) DERMAL RES LAB INC
CYC 1
PI US 5888984 A 19990330 (199920)* 14p A61K031-715
ADT US 5888984 A US 1994-241692 19940512
PRAI US 1994-241692 19940512
IC ICM A61K031-715
ICS A61K031-70; A61K031-725; A61K035-78
AB US 5888984 A UPAB: 19990525

Topical composition (I) comprises: (a) at least one low purity or cosmetic grade complex carbohydrate selected from oligosaccharides, silylated oligosaccharides, polysaccharides and glycosaminoglycans; and (b) at least one essential oil which can penetrate the dermis of mammals.

USE - (I) is used in the treatment of pain, inflammation and/or itching, preferably resulting from arthritis, bursitis, athletic injuries, tendonitis, trauma, poor circulation, tired feet, **allergies**, poison ivy, insect bites/stings, sunburn, burns, oedema related to diabetes, decubitus ulcers, dry skin, psoriasis, bruising, muscle cramping, superficial cuts and scrapes or open wounds. (I) is in the form of an emulsion, suspension, solution, cream or ointment (all claimed). (I) can be used in the treatment of humans, dogs, cats, horses, cattle and swine.

ADVANTAGE - The complex carbohydrates used, attach to various receptor sites on leukocytes, such as CD44, effectively blocking the adhesion cascade (the mechanism by which inflammation is produced).

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-B01C1; B04-C02E; B04-C02X; B04-D01; B12-M02B; B14-C01; B14-C03; B14-F02; **B14-G02A**; B14-N17; B14-S12

L133 ANSWER 5 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-120512 [10] WPIDS
DNC C1999-035205
TI Use of hyaluronidase for treatment of inflammation - useful for, e.g. delaying rejection of immunosuppressed **allograft**.
DC B04 D16
IN GERDIN, B; HAELLGREN, R; JOHNSSON, C; TUFVESON, G
PA (GERD-I) GERDIN B; (HALL-I) HALLGREN R; (JOHN-I) JOHNSSON C; (TUFV-I) TUFVESON G; (HAEL-I) HAELLGREN R
CYC 82
PI WO 9902181 A1 19990121 (199910)* EN 14p A61K038-47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
SE 9702657 A 19990110 (199915) A61K038-47
AU 9874618 A 19990208 (199924) A61K038-47
ADT WO 9902181 A1 WO 1998-SE831 19980506; SE 9702657 A SE 1997-2657 19970709; AU 9874618 A AU 1998-74618 19980506
FDT AU 9874618 A Based on WO 9902181
PRAI SE 1997-2657 19970709
IC ICM A61K038-47
ICS C12N009-26
AB WO 9902181 A UPAB: 19990310
Use of hyaluronidase (I) for the manufacture of a drug for treatment of inflammation associated with an increased local synthesis of **hyaluronan** (II) is new. Also claimed is a method for treatment inflammatory conditions associated with an increased local synthesis of (II) comprising systemic or local treatment with (I).

USE - (I) is used to treat inflammation in connection with organ grafting. (I) delays rejection of a non-immunosuppressed allograft and reduces inflammatory cell infiltrates, acting as a magnet for inflammatory cells. (I) is used to treat inflammatory conditions associated with an organ graft of e.g. a liver, kidney or heart of mammalian origin, including human origin.

Dwg.0/0

FS CPI
FA AB
MC CPI: B04-L05B; B14-C03; D05-A02C; D05-C03C

L133 ANSWER 6 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-059715 [05] WPIDS

DNC C1999-017551
TI **Immunopotentiating** composition - comprises an antigen or antigen inducing substance and an immunoactive substance.
DC A96 B04 C06 D16
IN BRANDON, M R; FUJIOKA, K; LOFTHOUSE, S; NAGAHARA, S; NASH, A D; SANO, A
PA (KOKE) KOKEN KK; (SUMU) SUMITOMO PHARM CO LTD; (UYME) UNIV MELBOURNE; (SUMU) SUMITOMO SEIYAKU KK
CYC 83
PI WO 9852605 A1 19981126 (199905)* EN 80p A61K039-39
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS KE KG KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
ZA 9804103 A 19990224 (199913) 76p A61K000-00
AU 9872385 A 19981211 (199917) A61K039-39
JP 11193246 A 19990721 (199939) 29p A61K039-39
EP 983088 A1 20000308 (200017) EN A61K039-39
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9852605 A1 WO 1998-JP2172 19980518; ZA 9804103 A ZA 1998-4103 19980515; AU 9872385 A AU 1998-72385 19980518; JP 11193246 A JP 1998-155343 19980519; EP 983088 A1 EP 1998-919633 19980518, WO 1998-JP2172 19980518
FDT AU 9872385 A Based on WO 9852605; EP 983088 A1 Based on WO 9852605
PRAI JP 1997-316285 19971030; JP 1997-145920 19970519; JP 1997-142461 19970530
IC ICM A61K000-00; A61K039-39
ICS A61K009-00; A61K039-00; A61K047-30
AB WO 9852605 A UPAB: 19990203
Immunopotentiating composition comprises: (i) an antigen or antigen-inducing substance; (ii) a carrier comprising biocompatible material; and optionally (iii) a substance having immunoactivating, immunostimulating or immunomodulating activity. Also claimed is a method of producing an antibody (Ab) comprising administering the above composition to a mammal other than a human or to a bird to modulate the immune response and recovering the Ab.

USE - The method is useful in humans, other mammals and birds for increasing an immune response derived from an antigen. The method is used in human or veterinary medicine for preventing or treating diseases caused by antigens such as cholera, pertussis, plague, typhoid fever, meningitis, pneumonia, leprosy, gonorrhoea, dysentery, polio, gram-negative sepsis, colibacillemia, rabies, diphtheria, botulism, tetanus, poliomyelitis, influenza, Japanese encephalitis, rubella, measles, yellow fever, parotiditis, hepatitis A, hepatitis B, hepatitis C, varicella/herpes zoster, malaria, tuberculosis, candidiasis, dental caries, AIDS, cancer, matitis, anthrax, brucellosis, caseous lymphadenitis, enterotoxaemia, enteritidis, black disease, malignant oedema, black leg, leptospirosis, scabby mouth, vibrosis, erysipelas, strangles, bordetella, bronchitis, distemper, panleucopoenia, rhinotracheit, viral diarrhoea and pimelea poisoning or diseases caused by e.g. Staphylococcus aureus, S. Epidermidis, salmonellae, group B meningococci or streptococci, adenovirus and coronavirus.

Dwg.1/12
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C01; C04-C01; B04-C02; C04-C02; B04-C03; C04-C03; B04-E01; C04-E01; B04-E08; C04-E08; B04-F02; C04-F02; B04-F10; C04-F10; B04-F11; C04-F11; B04-G07; C04-G07; B04-G08; C04-G08; B04-G09; C04-G09; B04-H01; C04-H01; B04-H06; C04-H06; B04-N02; C04-N02; **B14-G01**; **C14-G01**; D05-H07; D05-H11

L133 ANSWER 7 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-541790 [46] WPIDS
CR 1994-311808 [39]; 1998-582594 [49]; 1999-600534 [51]
DNC C1998-162745
TI Composition containing keratinocyte **growth** factor - used for

proliferation and **growth** of non-keratinocyte epidermal cells after wounding or disease.

DC A96 B04 D16
IN HOUSLEY, R M; MORRIS, C F; PIERCE, G F
PA (AMGE-N) AMGEN INC
CYC 1
PI US 5814605 A 19980929 (199846)* 37p C07K014-71
ADT US 5814605 A CIP of US 1993-40742 19930326, Div ex US 1994-312483 19940926, US 1995-484065 19950606
PRAI US 1994-312483 19940926; US 1993-40742 19930326; US 1995-484065 19950606
IC ICM C07K014-71
ICS A61K038-18
AB US 5814605 A UPAB: 19991210
A new pharmaceutical composition comprises a keratinocyte growth factor (KGF) and a non-aqueous carrier.

USE - The composition can be used to stimulate the growth and differentiation of cells, other than keratinocytes, to regenerate damaged or diseased cells and tissues. KGF, a mitogen, preferably produced by recombinant means, has been found to stimulate in vivo proliferation of cells such as hair follicles and liver cells, amongst others. It can be used to treat abnormalities of adnexal structures (e.g. chemotherapy-induced alopecia and epidermolysis bullosa), regeneration of glandular mucosa caused by gastric ulcers, regeneration of lung tissue after smoke and fire damage, liver regeneration (e.g. after cirrhosis, failure or hepatitis), and inflammatory bowel diseases (e.g. Crohn's disease and ulcerative colitis).

Dwg.0/24
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-H06A; B14-E08; B14-E10C; B14-K01; B14-N12; B14-N17; B14-N17B; B14-R02; D05-H14A1; D05-H17A2

L133 ANSWER 8 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-239211 [21] WPIDS
CR 1988-161497 [23]; 1990-348275 [46]; 1990-348276 [46]; 1993-152202 [18]; 1998-332141 [29]; 1998-505583 [43]
DNN N1998-189209 DNC C1998-074646
TI Cell-**scaffold** composition, for growing cartilage in vivo - comprises a three-dimensional **scaffold** of biodegradable, synthetic polymer fibres and cartilage-producing cells attached to fibre surface.
DC A96 B04 D16 D22 P32
IN LANGER, R S; VACANTI, C A; VACANTI, J P
PA (CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC 1
PI US 5736372 A 19980407 (199821)* 17p C12N011-08
ADT US 5736372 A CIP of US 1986-933018 19861120, CIP of US 1987-123579 19871120, CIP of US 1989-339155 19890417, US 1990-509952 19900416
FDT US 5736372 A CIP of US 5041138
PRAI US 1990-509952 19900416; US 1986-933018 19861120; US 1987-123579 19871120; US 1989-339155 19890417
IC ICM C12N011-08
ICS A61F002-18; A61F002-28; C12N005-00
AB US 5736372 A UPAB: 19981028
The following are claimed: (A) a cell-scaffold composition for growing cells to produce a functional cartilaginous structure in vivo, comprising: (a) a fibrous three-dimensional scaffold, which is composed of fibres of a biodegradable, synthetic polymer, and (b) cartilage-producing cells, which are attached to the surface of the fibres of the scaffold, and which are attached uniformly throughout the scaffold. The fibres are spaced apart, so that the average interfibre distance is 100-300 mu m. The fibres provide sufficient surface area to allow attachment of a density of cells which is sufficient to produce the functional cartilaginous structure in vivo. Diffusion in the scaffold provides free exchange of nutrients, gases and waste to and from the cells, so that cell viability can be maintained

throughout the scaffold prior to formation of the functional cartilage in vivo; (B) a cell-scaffold composition comprising: (a) a fibrous three-dimensional scaffold, which is composed of fibres of a synthetic polymer, and (b) cartilage-producing cells, which are attached to the surface of the fibres of the scaffold, and which are attached uniformly throughout the scaffold. The fibres are separated by a distance sufficient to allow (i) multiple layers of cells to adhere to the surface of the fibres and (ii) to provide free exchange (by diffusion) of nutrients and waste to the attached cells, when the cells on the scaffold are cultured in a nutrient medium. The scaffold is in the form of an ear, a nose, or a component of an ear or a nose.

The polymer is a polyanhydride, polyorthoester, polyglycolic acid, polylactic acid and/or their copolymer. The scaffold is formed from a combination of biodegradable and non-biodegradable materials. The non-biodegradable material is polytetrafluoroethylene, nylon, ethylene vinyl acetate and/or a polyester. The composition also comprises a coating on the fibres. The coating is a basement membrane component, agar, agarose, gelatin, a glycosaminoglycan a collagen, gum arabic, fibronectin, laminin, **hyaluronic acid** and/or an attachment peptide.
The cells are chondrocyte cells, fibroblast cells capable of differentiation into chondrocytes, or bone precursor cells capable of differentiation into chondrocytes.

USE - The cell scaffold compositions may be used for production of joint relinings, growth of elastic cartilage for plastic or reconstructive replacement of cartilage structures (e.g. the ear or the nose), or for repair of large bone defects.

ADVANTAGE - The compositions can be cast or molded into desired shapes, or can be manipulated at the time of implantation. The cells can retain their normal morphology and cell function.

Dwg.0/10

FS CPI GMPI
FA AB; DCN
MC CPI: A12-V01; B04-C03B; B04-C03D; B04-F02; **B14-N01**; B14-N02; B14-N04; D05-H08; D09-C01C

L133 ANSWER 9 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-179176 [16] WPIDS
DNC C1998-057563
TI Treating interstitial oedema associated with **organ grafts** - using hyaluronidase which reduces elevated **hyaluronan**, and thus water, contents in connective tissue.
DC B04 D16
IN HALLGREN, R; JOHNSSON, C; TUFVESON, G; WAHLBERG, J; HAELLGREN, R
PA (HALL-I) HALLGREN R; (JOHN-I) JOHNSSON C; (TUFV-I) TUFVESON G; (WAHL-I) WAHLBERG J; (HAEL-I) HAELLGREN R
CYC 79
PI WO 9808538 A1 19980305 (199816)* EN 17p A61K038-47
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
SE 9603082 A 19980227 (199820) A61K038-47
AU 9737908 A 19980319 (199831) A61K038-47
SE 509350 C2 19990118 (199909) A61K038-47
NO 9900898 A 19990225 (199923) A61K000-00
EP 942745 A1 19990922 (199943) EN A61K038-47
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI
ADT WO 9808538 A1 WO 1997-SE1313 19970724; SE 9603082 A SE 1996-3082 19960826; AU 9737908 A AU 1997-37908 19970724; SE 509350 C2 SE 1996-3082 19960826; NO 9900898 A WO 1997-SE1313 19970724, NO 1999-898 19990225; EP 942745 A1 EP 1997-934835 19970724, WO 1997-SE1313 19970724
FDT AU 9737908 A Based on WO 9808538; EP 942745 A1 Based on WO 9808538
PRAI SE 1996-3082 19960826

IC ICM A61K000-00; A61K038-47
ICS C12N009-26
AB WO 9808538 A UPAB: 19980421
Use of hyaluronidase (I) for treating interstitial oedema associated with organ grafts and caused by increased local content of **hyaluronan** (II) in the connective tissue of a human or non-human mammal, is new.
USE - (I) is used to cure or prevent interstitial oedema, e.g. in kidney, liver or heart **transplants**. More generally (not claimed) (I) can be used wherever there is an increased local synthesis of (II), not exclusively in organ grafts. (I) is administered locally or systemically, at 1-100000 (especially 500-10000) international units (IU)/kg/day.
ADVANTAGE - (I) acts selectively in inflamed tissues; it degrades (II), causing release of excess water.
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-L05B; B14-N17B; D05-A02; D05-H09

L133 ANSWER 10 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-535380 [49] WPIDS
DNN N1997-445781 DNC C1997-171087
TI **Topical** anti-hyperalgesic film-forming composition - useful for treating peripheral hyperalgesia and inhibiting post-injury pain..
DC A96 B02 B03 B07 D22 P34
IN BALOGH, I; FARRAR, J J; KUMAR, V; MAYCOCK, A L
PA (ADOL-N) ADOLOR CORP
CYC 71
PI WO 9733634 A1 19970918 (199749)* EN 42p A61L025-00
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
US 5667773 A 19970916 (199749) 11p A61K031-00
AU 9719847 A 19971001 (199805) A61L025-00
EP 888141 A1 19990107 (199906) EN A61L025-00
R: DE FR GB
ADT WO 9733634 A1 WO 1997-US3315 19970226; US 5667773 A US 1996-614027 19960312; AU 9719847 A AU 1997-19847 19970226; EP 888141 A1 EP 1997-907990 19970226, WO 1997-US3315 19970226
FDT AU 9719847 A Based on WO 9733634; EP 888141 A1 Based on WO 9733634
PRAI US 1996-614027 19960312
REP FR 1589917; US 5288486
IC ICM A61K031-00; A61L025-00
ICS A61K007-40; A61K009-08; A61K047-30; A61K047-38
AB WO 9733634 A UPAB: 19990525
A topical anti-hyperalgesic composition for coating an injured or inflamed site is new. The composition comprises: (a) 1-65% of an anti-hyperalgesic compound incorporated in a film-forming polymeric material; (b) 1-76% of film-forming polymeric material which is capable of forming a continuous film at pH 5.5-8.5 and which contains O, N or S atoms in combination with Ca2+, Mg2+, Zn2+ or Ba2+ in a ratio in the range 7.7 to 1; and (c) 23-34% of aqueous carrier.
The film forming material is: (a) anionic carboxylated polysaccharides of an anionic carboxylated polysaccharide of pectin (D-galacturonoglycan), algin (anhydro-D-mannuronic acid and anhydro-L-guluronic acid residues), gum karaya (D-galacturonic acid, D-galactose or L-rhamnose); (b) anionic sulphonated synthetic polymer of polystyrene or polyaryl sulphone; and (c) cationic aminopolysaccharides of keratosulphate, chondroitin sulphate, hyaluronic sulphate, heparin, chitin or dermatan sulphate.
USE - The composition is useful for treating peripheral hyperalgesia and is useful for inhibiting post-injury pain associated with local inflammatory conditions including inflammation following infection, blisters, boils, acute skin injuries, abrasions, burns, cuts, contusions, surgical incisions, irritations, poison ivy, **allergic** rashes,

dermatitis, stings, bites and inflammation of joints.
ADVANTAGE - The composition has no effect on the central nervous system.
Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: A12-V01; A12-V03A; B04-C03; B06-D06; B07-D05; B12-M02D; B14-C01; B14-C03; **B14-G02A**; B14-N17; D09-C04B
ABEQ US 5667773 A UPAB: 19971211
Topical anti-hyperalgesic film-forming composition, for coating an injured/inflamed site on a mammalian patient to reduce hyperalgesia at the site, comprises: (a) 1-65 wt.% of an antihyperalgesic compound, which is devoid of central nervous system side effects; (b) 1-76 wt.% of a film forming polymeric material; and (c) 23-34 wt.% of an aqueous carrier. The film-forming material is capable of forming a continuous film at a pH of 5.5-8.5. The polymeric material has atoms (selected from N, O and S) containing polarisable electrons, in combination with a divalent cation (selected from Ca2+, Mg2+, Zn2+ and Ba2+). The ratio of the atoms containing the polarisable electrons to the divalent cations is 7.7 to 1. The film-forming material is selected from sodium ethylcellulose sulphate, sodium cellulose acetate sulphate, sodium carboxyethyl cellulose, chondroitin sulphate, dermatan sulphate, keratosulphate, **hyaluronic acid**, heparin, chitin, polyvinyl pyrrolidone, polyvinyl alcohol and polyethylene oxide.
USE - The composition is useful in treating post-injury pain associated with local inflammatory conditions, including inflammation following infection, blisters, boils, acute skin injuries, abrasions, burns, cuts, contusions, surgical incisions, irritations from various sources, poison ivy, **allergic** rashes, dermatitis, stings, bites and inflammation of joints.
Dwg.0/0

L133 ANSWER 11 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-503092 [46] WPIDS
DNN N1997-419296 DNC C1997-160027
TI Device to promote wound tissue regeneration in correct orientation - uses encasement element, mechanical guide for cell **growth** and agent that prevents formation of fibrin network.
DC A96 B04 B07 C03 C07 D16 D22 P32 P34
IN HANSSON, H
PA (HANS-I) HANSSON H
CYC 77
PI WO 9737002 A1 19971009 (199746)* EN 68p C12N005-06
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9723157 A 19971022 (199808) C12N005-06
NO 9804534 A 19981125 (199906) C12N005-06
CZ 9803067 A3 19990113 (199908) C12N005-06
BR 9708459 A 19990413 (199921) C12N005-06
CN 1219965 A 19990616 (199942) C12N005-06
EP 942960 A1 19990922 (199943) EN C12N005-06
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
HU 9902451 A2 19991129 (200003) C12N005-06
ADT WO 9737002 A1 WO 1997-SE565 19970401; AU 9723157 A AU 1997-23157 19970401; NO 9804534 A WO 1997-SE565 19970401, NO 1998-4534 19980928; CZ 9803067 A3 WO 1997-SE565 19970401, CZ 1998-3067 19970401; BR 9708459 A BR 1997-8459 19970401, WO 1997-SE565 19970401; CN 1219965 A CN 1997-195054 19970401; EP 942960 A1 EP 1997-915831 19970401, WO 1997-SE565 19970401; HU 9902451 A2 WO 1997-SE565 19970401, HU 1999-2451 19970401
FDT AU 9723157 A Based on WO 9737002; CZ 9803067 A3 Based on WO 9737002; BR 9708459 A Based on WO 9737002; EP 942960 A1 Based on WO 9737002; HU 9902451 A2 Based on WO 9737002
PRAI SE 1996-1243 19960329

REP 6.Jnl.Ref; EP 645149; US 4778467; US 4955893; US 4963146; US 5019087; US 5292802; WO 8806871; WO 9005552; WO 9310806; WO 9520359; WO 9522301; WO 9602286
IC ICM C12N005-06
ICS A61F002-04; A61L031-00
AB WO 9737002 A UPAB: 19971119
Promoting wound tissue regeneration in correct orientation comprises: (a) an encasement structure (ES), implanted to encase the wound area; (b) a mechanical guide (MG) for regenerating tissue placed in the encased area and which extends in a predetermined direction, and (c) an agent (I), administered to the surface of the encased wound area, that inhibits formation of a fibrin network. Also new is an implantable device comprising outer ES and inner gel structure with at least 1 guide channel for tissue regeneration which, when implanted, extends in the predetermined direction.

USE - The system is used to treat crush injuries and to promote regeneration in wounded nerves, tendons, ligaments, joint capsules, cartilages, bones, aponeurose or skeletal muscle tissue. The fibrin network formation inhibiting agent is in solution and an osmotic mini-pump, implanted subcutaneously, is provided for administering agent to the encased wound area (claimed).

ADVANTAGE - MG regeneration can be induced to occur in the required direction by inhibiting the formation of the fibrin network (claimed).

Dwg.2/8
FS CPI GMPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C01; C04-C01; B04-C02E2; C04-C02E2; B04-H06; C04-H06; B04-L01; C04-L01; **B14-F04**; **C14-F04**; B14-N17B; C14-N17B; **D05-H**; D09-C04B

L133 ANSWER 12 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-456762 [42] WPIDS
CR 1994-293954 [36]; 1996-159656 [16]; 1997-331543 [30]; 1997-332006 [30]; 1997-384623 [35]; 1997-469491 [43]; 1998-239842 [21]; 1998-348021 [30]
DNC C1997-145768
TI Preparation of **immunostimulant** suspensions - by sonication in aqueous medium containing di sulphide-crosslinkable polymer.
DC A96 B04 B07
IN DESAI, N P; GRINSTAFF, M W; SANDFORD, P A; SOON-SHIONG, P; SUSLICK, K S; WONG, M
PA (VIVO-N) VIVORX PHARM INC
CYC 1
PI US 5665383 A 19970909 (199742)* 32p A61K009-127
ADT US 5665383 A CIP of US 1993-23698 19930222, CIP of US 1993-35150 19930326, CIP of US 1994-200235 19940222, US 1995-488804 19950607
FDT US 5665383 A CIP of US 5362478, CIP of US 5439686, CIP of US 5498421
PRAI US 1995-488804 19950607; US 1993-23698 19930222; US 1993-35150 19930326; US 1994-200235 19940222
IC ICM A61K009-127
AB US 5665383 A UPAB: 20000124
Preparation of an immunostimulant for in-vivo delivery comprises subjecting an aqueous medium containing the immunostimulant and a biocompatible material capable of being crosslinked by disulphide bonds to high-intensity ultrasound for a time sufficient to promote crosslinking of the biocompatible material, whereby the drug is contained within a polymeric shell having a maximum cross-sectional diameter of 10 mu or less.

USE - Agents are immunostimulants, especially vaccines, for oral, intravenous, subcutaneous, intraperitoneal, intrathecal, intramuscular, intracranial, inhalational, topical, transdermal, rectal (suppository) or vaginal (pessary) administration, especially where the drug is an analgesic selected from acetaminophen, aspirin, ibuprofen and morphine.

ADVANTAGE - The suspensions have better stability than simple emulsions and contain no potentially allergenic emulsifiers. The polymer shell provides organ-targetting specificity (e.g liver, spleen, lung) due to uptake by the reticuloendothelial system.

Dwg.1/3
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-A04; B04-B04D2; B04-J03A; B04-N02; B10-C03; B10-C04C; B10-D03; B14-C01; **B14-G01**; B14-S11

L133 ANSWER 13 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-435541 [40] WPIDS
DNC C1997-139756
TI Medicaments for targetting cells expressing **hyaluronic acid** receptors - contain **gene therapy** agent and **hyaluronic acid**.
DC B04 D16
IN ASCULAI, S S; TURLEY, E A
PA (HYAL-N) HYAL PHARM CORP
CYC 72
PI ZA 9608847 A 19970730 (199740)* 38p A61K000-00
WO 9817320 A1 19980430 (199823)# EN 37p A61K048-00
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9672721 A 19980515 (199838)# A61K048-00
EP 952855 A1 19991103 (199951)# EN A61K048-00
R: DE FR GB IT SE
ADT ZA 9608847 A ZA 1996-8847 19961022; WO 9817320 A1 WO 1996-CA700 19961018; AU 9672721 A AU 1996-72721 19961018, WO 1996-CA700 19961018; EP 952855 A1 EP 1996-934250 19961018, WO 1996-CA700 19961018
FDT AU 9672721 A Based on WO 9817320; EP 952855 A1 Based on WO 9817320
PRAI ZA 1996-8847 19961022; WO 1996-CA700 19961018; AU 1996-72721 19961018; EP 1996-934250 19961018
IC ICM A61K000-00; A61K048-00
ICS A61K031-70; A61K031-715; C12N015-11
ICA C12N015-87
AB ZA 9608847 A UPAB: 19971006
Pharmaceutical compositions containing a gene therapy agent associated with/bound to **hyaluronic acid** (HA) or a **hyaluronate** salt, are new.

The HA has a molecular wt. of 150-750 kDa. The HA is **sodium hyaluronate**. The HA dose is >50 (preferably at least 500) mg/70 kg person. The RNA-DNA oligonucleotide hybrid comprises a DNA oligonucleotide protected at both ends by RNA.

USE - The compositions are used for delivery of gene therapy agents, either antisense molecules or therapeutic genomic DNA, cDNA, oligonucleotides, RNA-DNA oligonucleotide hybrids or mRNA, to target cells that express HA receptors, e.g. CD44 or receptor for **hyaluronan** -mediated motility (RHAMM). The compositions are sterile. They are administered systemically, preferably by injection, especially intravenously, or are administered topically or directly to the tissue to be treated.

ADVANTAGE - The targeting effect of the HA allows doses of the gene therapy agent to be reduced.

Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-B03C; B04-C02; B04-E02; B04-E06; B14-S03; D05-H12

L133 ANSWER 14 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-259541 [24] WPIDS
DNC C1997-083916
TI **Modulation** of cellular activity - with **hyaluronic acid** is useful for treatment of colds, strokes, inflammatory processes, fibrosis and oncogene control.
DC A96 B04 D16
IN ASCULAI, S S

PA (HYAL-N) HYAL PHARM CORP
CYC 1
PI CA 2156013 A 19970215 (199724)* EN 46p A61K031-725
ADT CA 2156013 A CA 1995-2156013 19950814
PRAI CA 1995-2156013 19950814
IC ICM A61K031-725
AB CA 2156013 A UPAB: 19970612
Method for the modulation of cellular activity of tissue and cells, expressing a high affinity cell-surface receptor for a form of **hyaluronic acid** (e.g. an adhesion molecule, especially ICAM-1, HARLEC or CD44 and/or a regulatory molecule, especially RHAMM) in humans, comprises administering a form of **hyaluronic acid**, e.g. **hyaluronic acid**, its salt, e.g. **sodium hyaluronate** with molecular weight < 750 (especially 225) kDa, fractions, homologues, analogues, derivatives, complexes, esters, fragments and/or subunits of **hyaluronic acid** and/or a molecule which mimics the forms of **hyaluronic acid**.

Also claimed is a pharmaceutical composition containing the substances listed above together with a therapeutic agent to treat disease and an excipient.

USE - The method is useful for the treatment and prevention of diseases such as a cold, a stroke, inflammatory processes, fibrosis and oncogene control (all claimed).

The dosage is 10-1000 (preferably 50-500) mg.

Dwg.0/8
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C02; B14-C03; **B14-H01**; B14-N16; **D05-H**

L133 ANSWER 15 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-212668 [19] WPIDS
DNC C1997-068659
TI Use of **hyaluronic acid** for inhibiting T-cell activity - and treating e.g. autoimmune diseases and **graft** rejection following **transplant**.
DC B04
IN BUELOW, R; LUSSOW, A R
PA (SANG-N) SANGSTAT MEDICAL CORP
CYC 75
PI WO 9711710 A1 19970403 (199719)* EN 25p A61K031-725
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9671191 A 19970417 (199732) A61K031-725
EP 852501 A1 19980715 (199832) EN A61K031-725
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11500742 W 19990119 (199913) 26p A61K031-725
US 6013641 A 20000111 (200010) A01N043-04
ADT WO 9711710 A1 WO 1996-US15514 19960927; AU 9671191 A AU 1996-71191 19960927; EP 852501 A1 EP 1996-932347 19960927, WO 1996-US15514 19960927; JP 11500742 W WO 1996-US15514 19960927, JP 1997-513668 19960927; US 6013641 A Provisional US 1995-4468 19950928, US 1996-721835 19960927
FDT AU 9671191 A Based on WO 9711710; EP 852501 A1 Based on WO 9711710; JP 11500742 W Based on WO 9711710
PRAI US 1995-4468 19950928; US 1996-721835 19960927
REP 3.Jnl.Ref; WO 8705517; WO 9104058
IC ICM A01N043-04; A61K031-725
AB WO 9711710 A UPAB: 19990416
A method of inhibiting graft rejection following **transplantation** or other T-cell activity comprises admin. of a compsn. contg. D-glucuronic beta (1-3) N-acetyl-D-glucosamine polymers (I).

USE - T-cell mediated conditions which can be treated by the admin. of **hyaluronic acid** include autoimmune diseases, e.g.

multiple sclerosis, rheumatoid arthritis, psoriasis, pemphigus vulgaris, Sjogren's disease, thyroid disease, Hashimoto's thyroiditis, myasthenia gravis; also graft versus host disease. (I) can be administered in combination with other active agents, e.g. immunosuppressants.
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: B04-C02; B14-C09B; **B14-G02C**; B14-G02D; B14-N11; B14-N17C; B14-S01

L133 ANSWER 16 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-131802 [12] WPIDS
CR 1999-493513 [41]
DNC C1997-042511
TI Maintaining hepatocyte(s) in culture - by contacting with support contg. sterilised collagen, used to replace or **augment** liver function.
DC B04 D16
IN DUNN, J; TOMPKINS, R G; YARMUSH, M L
PA (GEHO) GEN HOSPITAL CORP; (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC 1
PI US 5602026 A 19970211 (199712)* 7p C12N005-02
ADT US 5602026 A Cont of US 1988-258309 19881014, Cont of US 1991-717857 19910619, US 1994-331167 19941028
PRAI US 1988-258309 19881014; US 1991-717857 19910619; US 1994-331167 19941028
IC ICM C12N005-02
ICS C12N005-00
AB US 5602026 A UPAB: 19991011
Maintaining hepatocytes in culture comprises contacting the hepatocytes with a support comprising 2 layers, where the support comprises sterilised collagen and has a configuration that permit each of at least a portion of the hepatocytes to form at least 1 apical surface and at least 2 discrete basal surfaces, where < 1% of cells present in the culture are non-hepatocytic cells. Also claimed is a method for maintaining hepatocytes in culture which comprises immobilising the hepatocytes within collagen beads having a configuration as above.
USE - The culture hepatocytes can be used for transplantation. Hepatocytes maintained according to the method can be used to replace or augment liver function by constructing a bioreactor having metabolic functions of the liver in vivo, and then either implanting the bioreactor into a recipient animal such as a patient having impaired liver function, or maintaining the bioreactor outside the body as an extra corporeal perfusion system. Hepatocytes supported in this way can be arranged and configured to permit an exchange or a flow of medium, such as a perfusate such as blood or blood plasma, or a culture medium from which a prod. of hepatocyte metabolism, such as clotting factors, can be recovered, or a fluid from which a substance can be removed by the metabolic activity of the hepatocytes.
ADVANTAGE - Entrapment of the hepatocytes in e.g. collagen helps prevent graft rejection and the addn. of extracellular matrix prods. such as collagen to cultures of hepatocytes can improve maintenance of differentiated functions.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-F02; B04-N02; **B14-G02C**; B14-N12; D05-H08

L133 ANSWER 17 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-384212 [38] WPIDS
DNC C1996-120888
TI Sulphated muco-poly saccharide or dextran derivs. are anti-inflammatory agents - also used for healing ischaemic heart disease and infiltration following **organ transplantation**.
DC B04
IN AKIMA, K; MIYASAKA, M; SUZUKI, Y; WARD, P A
PA (SHIS) SHISEIDO CO LTD

CYC 19
PI WO 9624362 A1 19960815 (199638)* JA 20p A61K031-725
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: US
JP 08277224 A 19961022 (199701) 5p A61K031-725
EP 754460 A1 19970122 (199709) EN 7p A61K031-725
R: CH DE FR GB IT LI
EP 754460 A4 19970409 (199735) A61K031-725
US 5872109 A 19990216 (199914) A01N043-04
ADT WO 9624362 A1 WO 1996-JP239 19960206; JP 08277224 A JP 1996-40309 19960205; EP 754460 A1 EP 1996-901544 19960206, WO 1996-JP239 19960206; EP 754460 A4 EP 1996-901544 ; US 5872109 A WO 1996-JP239 19960206, US 1996-722131 19961004
FDT EP 754460 A1 Based on WO 9624362; US 5872109 A Based on WO 9624362
PRAI JP 1995-41407 19950207
REP EP 420849; EP 536363; JP 4500797; JP 5235710; JP 5508184; JP 6107550; JP 62201825; JP 892103; WO 8905646; WO 9218545; EP 208623; EP 214879; EP 717995; WO 8807060; WO 9418989; WO 9426759; WO 9525751
IC ICM A01N043-04; A61K031-725
ICS C07H005-04
ICA C08B037-02; C08B037-08
AB WO 9624362 A UPAB: 19960924
Antiinflammatory agents comprise a sulphate mucopolysaccharide (SMP) or sulphated dextran (SD) deriv. or their salt. Also claimed is the use of SMP or SD derivs. for the treatment of adult respiratory distress syndrome (ARDS), ischaemic heart disease, cerebral ischaemia, chronic rheumatoid arthritis, atopic dermatitis and infiltration following organic **transplantation**.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C02; B14-C03

L133 ANSWER 18 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-277718 [28] WPIDS
CR 1990-224382 [29]
DNC C1996-088164
TI New ligand **matrix** for inducing tissue regeneration and wound healing - contains a ligand for the a.
DC B04 D16
IN RUOSLAHTI, E I; VUORI, K
PA (LJOL-N) LA JOLLA CANCER RES CENT; (LJOL-N) LA JOLLA CANCER RES FOUND
CYC 22
PI WO 9616983 A1 19960606 (199628)* EN 51p C07K007-08
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR
AU 9644123 A 19960619 (199640) C07K007-08
US 5654267 A 19970805 (199737) 21p A61K038-00
EP 797584 A1 19971001 (199744) EN C07K007-08
R: BE CH DE DK FR GB IT LI NL SE
JP 10509980 W 19980929 (199849) 45p C07K007-06
US 5830504 A 19981103 (199851) A61K038-04
ADT WO 9616983 A1 WO 1995-US15542 19951130; AU 9644123 A AU 1996-44123 19951130; US 5654267 A Cont of US 1988-286973 19881220, Cont of US 1992-978054 19921118, Cont of US 1993-142842 19931025, CIP of US 1994-176999 19940103, US 1994-347942 19941130; EP 797584 A1 EP 1995-942948 19951130, WO 1995-US15542 19951130; JP 10509980 W WO 1995-US15542 19951130, JP 1996-519043 19951130; US 5830504 A Cont of US 1988-286973 19881220, Cont of US 1992-978054 19921118, Cont of US 1993-142842 19931025, CIP of US 1994-176999 19940103, Cont of US 1994-347942 19941130, US 1995-456878 19950601
FDT AU 9644123 A Based on WO 9616983; EP 797584 A1 Based on WO 9616983; JP 10509980 W Based on WO 9616983
PRAI US 1994-347942 19941130; US 1988-286973 19881220; US 1992-978054 19921118; US 1993-142842 19931025; US 1994-176999 19940103; US 1995-456878 19950601

REP 01Jnl.Ref; US 4578079; US 4683291; US 4703108; US 5128326
IC ICM A61K038-00; A61K038-04; C07K007-06; C07K007-08
ICS A61K009-00; A61K038-10; A61K038-18; A61K038-20; A61K038-22; A61K038-28; A61K038-30; A61K038-39; A61K047-48; C07K014-49; C07K014-54; C07K014-62; C07K014-65; C07K014-78; C07K017-02; C07K017-10
AB WO 9616983 A UPAB: 19970922
A new compsn. comprises a first ligand (L1) to the alpha v beta 3 integrin and second ligand (L2) to the receptor of: platelet-deriv. growth factor (PDGF); insulin growth factor (GF); interleukin-4 (IL-4); and insulin-like GF, where both ligands are contained within a matrix.
USE - The L1 and L2 have a synergistic effect in enhancing wound healing, and the compsn. is used to promote cell attachment, migration and proliferation and to induce tissue regeneration at the wound site. The compsns. are also useful as matrices to support cell growth and tissue regeneration in vitro.
Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-C02B; B04-C02E; B04-C03C; B04-G02; B04-H02D; B04-H06B; B04-H20B; B04-J03A; B04-N02; B04-N04B; B14-N17B; B14-S09; D05-H10
ABEQ US 5654267 A UPAB: 19970915
A composition comprising a substantially purified first ligand to an alpha v beta 3 integrin and a substantially purified second ligand selected from the group consisting of a ligand to a PDGF receptor, a ligand to an insulin receptor, a ligand to an IL-4 receptor, and a ligand to an insulin-like growth factor receptor, wherein said first ligand and said second ligand are incorporated within a matrix, and wherein the combination of said first ligand and said second ligand results in a synergistic effect on cell proliferation or cell migration.
Dwg.0/6

L133 ANSWER 19 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-251551 [25] WPIDS
DNC C1996-079591
TI Liposome compsn. contg. superoxidedismutase and opt. **hyaluronic acid** - for treatment of burns, radiation damage, bronchitis, acne, inflammation etc., and preservation of **transplant organs**, foodstuffs, etc..
DC B04 D13 D16 D21 D22
IN FURNSCHLIEF, E; KATINGER, H; VORAUER-UHL, K; FUERNSCHLIEF, E; VORAUERUHL, K
PA (POLY-N) POLYMUN SCI IMMUNOBIOLOGISCHE FORSCHUNG
CYC 68
PI WO 9614083 A1 19960517 (199625)* DE 40p A61K038-44
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9539816 A 19960531 (199639) A61K038-44
EP 789584 A1 19970820 (199738) DE A61K038-44
R: AT BE CH DE ES FR GB IE IT LI PT
BR 9509590 A 19971223 (199806) A61K038-44
AU 690377 B 19980423 (199828) A61K038-44
MX 9703184 A1 19971201 (199936) A61K038-44
US 5942245 A 19990824 (199941) A61K009-133
ADT WO 9614083 A1 WO 1995-EP4352 19951106; AU 9539816 A AU 1995-39816 19951106, WO 1995-EP4352 19951106; EP 789584 A1 EP 1995-938419 19951106, WO 1995-EP4352 19951106; BR 9509590 A BR 1995-9590 19951106, WO 1995-EP4352 19951106; AU 690377 B AU 1995-39816 19951106; MX 9703184 A1 MX 1997-3184 19970430; US 5942245 A WO 1995-EP4352 19951106, US 1997-836185 19970701
FDT AU 9539816 A Based on WO 9614083; EP 789584 A1 Based on WO 9614083; BR 9509590 A Based on WO 9614083; AU 690377 B Previous Publ. AU 9539816, Based on WO 9614083; US 5942245 A Based on WO 9614083

PRAI EP 1994-117409 19941104
REP 11Jnl.Ref; EP 207039; JP 01319427; JP 05097694; JP 63077824; WO 8701387
IC ICM A61K009-133; A61K038-44
ICS A23L001-015; C12N009-02
AB WO 9614083 A UPAB: 19960625
Elevated superoxide radical concn. and associated damage is prevented or treated by admin. of a liposomal compsn. contg. superoxide dismutase (SOD), pref. recombinant human SOD (rhSOD), opt. in admixture with **hyaluronic acid** and/or 1 carrier and opt. other additives. Note: Non-recombinant SOD is excluded from claim 1, but disclosed in description. Also claimed is the use of the compsn. for improving the storage stability of organic, pref. biogenic, materials.
USE - The compsn. can be used esp. to prevent or treat radiation damage caused by UV or ionising radiation, burns, scalds, inflammatory skin disorders and other inflammations or inflammatory processes, including those caused by microbes, esp. viruses such as influenza and herpes viruses, osteoarthritis, respiratory diseases, esp. bronchitis, acute respiratory distress syndrome and emphysema, furuncles, acne, skin reddening and swelling, psoriasis. Admin. of the compsn. is by the oral, parenteral or topical route. Organic materials which can be treated with the compsn. to improve storage stability are esp. tissue and organs used in **transplants**, foods, esp. meat and milk prods., and organic based cosmetic preparations esp. skin care agents formulated as salves, creams, gels, oils, etc. The amt. of SOD used to protect such materials is pref. 0.1-100 mg/kg. Oral or parenteral SOD dose, pref. as a suspension, is 0.5-50 mg/kg. Topical treatment is pref. in a salve, cream or gel applied in a dose of 0.01-1 mg/cm2 (all claimed).
ADVANTAGE - The compsn. is gentle and effective and, in contrast to prior art SOD formulations, provides better bioavailability at the treatment site, esp. after topical admin. The SOD and **hyaluronic acid** exert a synergistic effect.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C02; B04-L03A; B14-C03; B14-N17A; B14-R05; D03-H01P; D05-A01A4; D05-A01B1; D08-B09A; D08-B11; D09-C04B; D09-E

L133 ANSWER 20 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-049281 [05] WPIDS
DNC C1996-016002
TI Treating **respiratory** disorders with **hyaluronic acid** - admin. intratracheally by instillation or aerosol e.g. in bronchitis or emphysema.
DC B04
IN CANTOR, J O
PA (CANT-I) CANTOR J O
CYC 21
PI WO 9526735 A1 19951012 (199605)* EN 33p A61K031-715
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP MX US
AU 9522040 A 19951023 (199606)
US 5633003 A 19970527 (199727) 11p A61K031-715
ADT WO 9526735 A1 WO 1995-US4059 19950330; AU 9522040 A AU 1995-22040 19950330; US 5633003 A US 1994-221866 19940331
FDT AU 9522040 A Based on WO 9526735
PRAI US 1994-221866 19940331
REP US 4119096; US 4649911; US 4851521; US 5049388
IC ICM A61K031-715
ICS A01N043-04
AB WO 9526735 A UPAB: 19960205
A respiratory disorder is treated by intratracheal administration to a mammal of **hyaluronic acid** (I).
USE - The disorder may be e.g. emphysema, chronic bronchitis, **asthma**, pulmonary oedema, acute respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary fibrosis or pulmonary atelectasis. The treatment is intended for a variety of mammals, but esp. for premature

neonates or adult humans.
Dwg.0/7
FS CPI
FA AB; DCN
MC CPI: B04-C02E; B12-M01A; B14-K01
ABEQ US 5633003 A UPAB: 19970702
Treating a respiratory disorder selected from emphysema, chronic bronchitis, **asthma**, pulmonary edema, acute respiratory distress syndrome, broncho-pulmonary dysplasia, pulmonary fibrosis and pulmonary atelectasis, comprises intra-tracheally administering a **hyaluronic acid**.
Dwg.0/5

L133 ANSWER 21 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-357924 [44] WPIDS
DNN N1994-280463 DNC C1994-163305
TI Compsn for implanting tissue into an animal - comprising hydrogel soln mixed with **dissociated** cells.
DC A96 B04 D16 D22 P32 P34
IN ATALA, A; GRIFFITH-CIMA, L; PAIGE, K T; VACANTI, C A
PA (CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC 21
PI WO 9425080 A1 19941110 (199444)* EN 53p A61L027-00
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9470157 A 19941121 (199508) A61L027-00
EP 708662 A1 19960501 (199622) EN A61L027-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 09500040 W 19970107 (199711) 45p A61L027-00
US 5667778 A 19970916 (199743) 9p A61K035-34
AU 684796 B 19980108 (199810) A61L027-00
US 5709854 A 19980120 (199810) 11p C12N005-08
US 5976526 A 19991102 (199953) A61K035-34
ADT WO 9425080 A1 WO 1994-US4710 19940429; AU 9470157 A AU 1994-70157 19940429; EP 708662 A1 EP 1994-919101 19940429, WO 1994-US4710 19940429; JP 09500040 W JP 1994-524555 19940429, WO 1994-US4710 19940429; US 5667778 A CIP of US 1993-56140 19930430, US 1994-228678 19940418; AU 684796 B AU 1994-70157 19940429; US 5709854 A US 1993-56140 19930430; US 5976526 A CIP of US 1993-56140 19930430, Cont of US 1994-228678 19940418, US 1997-919407 19970828
FDT AU 9470157 A Based on WO 9425080; EP 708662 A1 Based on WO 9425080; JP 09500040 W Based on WO 9425080; AU 684796 B Previous Publ. AU 9470157, Based on WO 9425080; US 5976526 A Cont of US 5667778, CIP of US 5709854
PRAI US 1994-229464 19940418; US 1993-56140 19930430; US 1994-228678 19940418; US 1997-919407 19970828
REP EP 344924; EP 361957; US 4846835; WO 9101720; WO 9206702; WO 9316687
IC ICM A61K035-34; A61L027-00; C12N005-08
ICS A61F002-02; C12N005-00; C12N005-06; C12N011-04; C12N011-10
AB WO 9425080 A UPAB: 19960610
Method for implanting tissue into an animal comprises mixing a biodegradable, biocompatible hydrogen soln. with dissociated cells and implanting the mixt. into the animal. Also claimed is a compsn. for implanting tissue into an animal, comprising a hydrogel soln. (I) mixed with dissociated cells.
USE - The method may be used to treat vesicoureteral reflux, urinary incontinence and other tissue defects.
ADVANTAGE - The method is quick, simple, safe and relatively non-invasive.
Dwg.0/1
FS CPI GMPI
FA AB; GI; DCN
MC CPI: A12-S; A12-V02; B04-C03; B04-F02; B14-N07D; B14-N17; D05-H08; D05-H09; D09-C
ABEQ US 5667778 A UPAB: 19971030
Method for treating conditions which require the reconstruction of an anatomical area selected from the thoracic region, gastrointestinal tract,

urinary tract, and reproductive tract. The method comprises injecting into a patient, at a site in the anatomical area, a suspension of smooth muscle cells in a biodegradable non-proteinaceous polymer solution that forms an ionically crosslinked hydrogel having the cells dispersed in it when injected in vivo, which becomes a non-migratory, volume stable tissue mass.
Dwg.0/1

ABEQ US 5709854 A UPAB: 19980309
Method for implanting tissue into an animal comprises mixing a biodegradable, biocompatible hydrogen soln. with dissociated cells and implanting the mixt. into the animal. Also claimed is a compsn. for implanting tissue into an animal, comprising a hydrogel soln. (I) mixed with dissociated cells.
USE - The method may be used to treat vesicoureteral reflux, urinary incontinence and other tissue defects.
ADVANTAGE - The method is quick, simple, safe and relatively non-invasive.
Dwg.0/0

L133 ANSWER 22 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-328983 [41] WPIDS
DNC C1994-149037
TI Cell **growth** stimulating compsns. stimulate **growth** of animal or microbial cells - contg. prod. obtd. by treating saccharide contg. uronic acid with uronic acid lyase.
DC B04 D16
PA (MEIJ) MEIJI SEIKA KAISHA
CYC 1
PI JP 06253830 A 19940913 (199441)* 10p C12N001-38
ADT JP 06253830 A JP 1993-69186 19930305
PRAI JP 1993-69186 19930305
IC ICM C12N001-38
ICS C12N005-06
AB JP 06253830 A UPAB: 19941206
Cell growth stimulating compsn. contains a component (A). (A) is obtained by the action of uronic acid lyase on a sugar (I) contg. a uronic acid, opt. in the presence of ammonium salt.
Pref. (I) is pectin, pectinic acid, alginic acid, **hyaluronic acid**, and their metals salts. The uronic acid is glucuronic acid, galacturonic acid. The uronic acid is glucuronic acid, galacturonic acid, mannuronic acid, gulonic acid, iduronic acid opt. in the form of the metals salts.
USE/ADVANTAGE - Stable growth stimulation of microbial and animal cells.
Uronic acids (e.g. glucuronic acid, galacturonic acid, mannuronic acid, gulonic acid, iduronic acid and their metal salts) contg. saccharides (e.g. pectin, pectinic acid, alginic acid, **hyaluronic acid**, chondroitin sulphate and their metal salts) are caused to react with uronic acid lyase (e.g. lyases of pectin, exo-polygalacturonic acid, pectinic acid, alginic acid and alginic acid) at ratios of 100-4,000 unit/g of saccharide for 12-48 hrs. pref. in the presence of 0.01 pts. of ammonium salt. The prod. is added to culture media of cells at 0.001-1.0, pref. 0.005-0.5 wt.%.
In an example, 100 g of pectin was dissolved in 1.5 L of drinking water. Pectin lyase was added at a rate of 2,000 U/g of pectin, and reacted at pH 5.5, 30 deg.C for 20 hrs. The lyase was deactivated by the addn. of 10 g of (NH4)2SO4 and heated at 90 deg.C for 10 min., condensed and lyophilised to give 115 g of prod. (A). Saccharomyces cerevisiae ATCC 26786 was cultured at 25 deg.C for 48 hrs. in a medium with 0.1% (A) and 8.4 x 10 power(-6) cells/ml were obtained, while a control gp. without (A) produced 4.5 x 10power(-6) cells.
Dwg.0/0
FS CPI
FA AB; GI
MC CPI: B04-C02D; B07-A02B; B14-E11; D05-A02; D05-H01

L133 ANSWER 23 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-234365 [28] WPIDS
DNC C1992-105676
TI Cell proliferation **matrix** contg. aq. gel of **hyaluronic acid** - for treating bone fractures, ulcus varicosum cruris and ulcers caused by diabetes mellitus.
DC B04 D16
IN ABERG, B; BRISMAR, K
PA (SKAN-N) SKANDIGEN AB
CYC 21
PI WO 9210195 A1 19920625 (199228)* 11p A61K031-715
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU BR CA JP KR US
SE 9003887 A 19920607 (199231) A61K031-715
AU 9190409 A 19920708 (199241) A61K031-715
EP 560845 A1 19930922 (199338) EN A61K031-715
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06503319 W 19940414 (199420) 5p A61K031-725
AU 649092 B 19940512 (199425) C12N005-00
SE 501217 B 19941212 (199504) A61K031-715
US 5432167 A 19950711 (199533) 4p A61K031-725
EP 560845 B1 19970827 (199739) EN 4p A61K031-715
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
DE 69127459 E 19971002 (199745) A61K031-715
ADT WO 9210195 A1 WO 1991-SE839 19911205; SE 9003887 A SE 1990-3887 19901206; AU 9190409 A AU 1991-90409 19911205, WO 1991-SE839 19911205; EP 560845 A1 WO 1991-SE839 19911205, EP 1992-900297 19911205; JP 06503319 W WO 1991-SE839 19911205, JP 1992-500592 19911205; AU 649092 B AU 1991-90409 19911205; SE 501217 B SE 1990-3887 19901206; US 5432167 A WO 1991-SE839 19911205, US 1993-66165 19930607; EP 560845 B1 WO 1991-SE839 19911205, EP 1992-900297 19911205; DE 69127459 E DE 1991-627459 19911205, WO 1991-SE839 19911205, EP 1992-900297 19911205
FDT AU 9190409 A Based on WO 9210195; EP 560845 A1 Based on WO 9210195; JP 06503319 W Based on WO 9210195; AU 649092 B Previous Publ. AU 9190409, Based on WO 9210195; US 5432167 A Based on WO 9210195; EP 560845 B1 Based on WO 9210195; DE 69127459 E Based on EP 560845, Based on WO 9210195
PRAI SE 1990-3887 19901206
REP 4.Jnl.Ref; EP 138572; EP 312208
IC ICM A61K031-715; A61K031-725
ICS A61K009-06; C08B037-08; C12N005-02
AB WO 9210195 A UPAB: 19931006
A cell proliferative matrix comprising an aq. gel of **hyaluronic acid** or its salts, free from prodn.-related animal DNA and RNA and in a dissolved state. The aq. gel may contain water or PBS.
Also claimed is the use of **hyaluronic acid** or its salts, free from prodn.-related animal DNA and RNA for the prepn. of an aq. cell proliferation matrix for the treatment of at least one of bone fractures, ulcus varicosum cruris and ulcers caused by diabetes mellitus and other diseases with impaired arterial blood flow, such as decubitus.
ADVANTAGE - The cell proliferation matrix promotes epithelial and endothelial cell growth and also osteoblast growth.
0/0
FS CPI
FA AB; DCN
MC CPI: B04-C02; B12-E01; B12-E08; **B12-J08**; D05-C08
ABEQ EP 560845 A UPAB: 19931123
Matrix comprises an aq. gel of **hyaluronic acid** or its salts, free from prodn.-related animal DNA and RNA and in a dissolved state. The aq. gel may contain water or PBS.
USE/ADVANTAGE - Used for the treatment of bone fractures, ulcus varicosum cruris and ulcers caused by diabetes mellitus and other diseases with impaired arterial blood flow, such as decubitus.The cell proliferation matrix promotes epithelial and endothelial cell growth and osteoblast growth.
ABEQ US 5432167 A UPAB: 19950824
A new treatment of Ulcus Varicosum or ulcers caused by Diabetes Mellitus

comprises topical admin. a cell proliferation matrix consisting of an aq. gel of dissolved **hyaluronic acid** or salt, obtd. from Streptococcus (pref. S. equiv). and free of animal DNA or RNA. The gel comprises 98.0-99.9% wt. water or phosphate buffered saline and 0.1-2.0 (1.0)% wt. **Na hyaluronate** of mean MW. at least 25000 Da. (1.2-3.5 x 10power6 Da).

USE - Treatment of bone fractures, Lucus Varicosum Cruris, ulcers caused by diabetes and other diseases with impaired arterial blood flow (Decubitus).

Dwg.0/0

ABEQ EP 560845 B UPAB: 19970926

Use of **hyaluronic acid** or a pharmaceutically acceptable salt thereof which is free from production-related animal DNA and RNA for the preparation of an aqueous cell proliferation matrix for the treatment of at least one of bone fractures, Ulcus Varicosum Cruris, and ulcera caused by Diabetes mellitus and other diseases with impaired arterial blood flow, such as Decubitus, wherein said aqueous cell proliferation matrix consists of a gel which is made of 99.9 to 98.0 percent by weight of water or of phosphate buffered saline solution and 0.1 to 2.0 percent by weight of **sodium hyaluronate** having an average molecular weight of 1.2 x 10 6 to 2.5 x 10 6 Da dissolved therein.

Dwg.0/0

L133 ANSWER 24 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-099827 [13] WPIDS
DNC C1992-046266
TI **Topically** administered **antiallergic** agents - contg. **hyaluronic acid**, used to treat **allergic** rhinitis, conjunctivitis and pollenosis.
DC B04
PA (SANT) SANTEN PHARM CO LTD
CYC 1
PI JP 04041431 A 19920212 (199213)* 4p
JP 2769584 B2 19980625 (199830) 3p A61K031-725
ADT JP 04041431 A JP 1990-146707 19900604; JP 2769584 B2 JP 1990-146707 19900604
FDT JP 2769584 B2 Previous Publ. JP 04041431
PRAI JP 1990-146707 19900604
IC A61K009-08; A61K031-72
ICM A61K031-725
ICS A61K009-08; A61K031-72; C08B037-08
AB JP 04041431 A UPAB: 19931006

Agents contain **hyaluronic acid** or its salts.

Also claimed is a pharmaceutical formulation comprising an eye drop contg **hyaluronic acid** or its salts and a pharmaceutical formulation comprising a nasal drop contg. **hyaluronic acid** or its salts.

The content of **hyaluronic acid** in the agents is pref. 0.01-0.5%, and adjuvants or additives may be added, including toxicity agents, buffers, preservatives, pH adjusters, etc.. The pH is pref. 5-8.

USE/ADVANTAGE - The agents have low toxicity, may be repeatedly applied for a prolonged period of time, and are useful in the treatment of **allergic** inflammations e.g. **allergic** rhinitis, conjunctivitis, pollenosis, or spring catarrh.

In an example a 100-ml (pH 6.5) formulation contained 0.1g **Na hyaluronate**, 0.75g NaCl, 0.15g KCl, 0.2g epsilon-aminocaproic acid 0.01g Na edetate, and NaOH.

0/0

FS CPI
FA AB; DCN
MC CPI: B04-C02E; **B12-D02**; B12-D07; B12-L04

L133 ANSWER 25 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1991-163945 [22] WPIDS

DNC C1991-070930
TI Compsns. contg. glycan(s) or monoclonal antibodies and enzymes - that inhibit their activity, used to inhibit and promote nerve **growth** or glial cell migration or invasion.
DC B04 D16
IN HAREL, A; ROUFA, D; SILVER, J; SNOW, D M
PA (GLIA-N) GLIATECH INC; (UYCA-N) UNIV CASE WESTERN RESERVE; (UYCA-N) CASE WEST UNIV; (GLIA-N) GLIA-TECH INC
CYC 32
PI WO 9106303 A 19910516 (199122)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE
W: AU BB BG BR CA DK ES FI HU JP KR LK MC MG MW NO RO SD SE SU
AU 9168726 A 19910531 (199135)
EP 493533 A1 19920708 (199228) EN 106p A61K031-715
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 06502840 W 19940331 (199418)# A61K031-725
EP 493533 A4 19921028 (199524)
ADT EP 493533 A1 EP 1990-917627 19901026, WO 1990-US6189 19901026; JP 06502840 W WO 1990-US6189 19901026, JP 1991-500439 19901026; EP 493533 A4 EP 1990-917627
FDT EP 493533 A1 Based on WO 9106303; JP 06502840 W Based on WO 9106303
PRAI US 1989-428374 19891027
REP US 1715098; US 4083960; US 4640912; US 4696816; US 4710493; US 4760131; US 4778768; US 4783447; US 4801619; US 4808570; US 4829000; US 4945086; US 4956348; 10Jnl.Ref; DE 3441835; EP 257003; WO 8801280; WO 9006755
IC ICM A61K031-715; A61K031-725
ICS A61K031-71; A61K037-48; A61K037-54; A61K037-56; A61K039-39; A61K039-395
AB WO 9106303 A UPAB: 19930928
The composition contains keratan sulphate, proteoglycan or glycosaminoglycan. Also claimed are compositions that contain chondrotin or dermatan proteoglycan or glycaosaminoglycan, and mixtures of these. The dermatan sulphate0 has a C-4 sulphur linkage, and the chondrotin sulphate has a C-6 sulphur linkage. The keratan sulphate may be type I (corneal) or type II (skeletal). Also claimed are compositions containing substances that destroy or antagonise the growth inhibiting function of these compounds. The substances are e.g. monoclonal antibodies selected from MZ15, 1/20/5-D-4, 4/8/1-B-4, 4-D-1 or 8-C-2, or enzymes such as endo-B-galactosidase, keratanase, chondroitinase or chondrotin ABC lyase. Also claimed are compositions containing heparin or **hyaluronate** disaccharide/ proteoglycan/glycosaminoglycan.

USE/ADVANTAGE - The compositions of keratan sulphate etc. can inhibit neurite outgrowth, i.e. axonal growth, and glial cell migration or invasion. Studies have shown that heparin inhibits attachment and neurite formation of human neuroblastoma cells on a cholera toxin B/ganglioside GM1-binding substratum (mungai et al, 1988, Exp. Cell Res. 175:299-247). The enzymes and monoclonal antibodies that antagonise the glycans growth inhibiting ability may be used to reverse nerve damage caused by trauma, surgery, sichaemia, infection, metabolic disease, nutritional deficiency, malignancy, exposure to toxins or degenerative disorders of the nervous system (claimed).
FS CPI
FA AB
ABEQ EP 493533 A UPAB: 19930928
The compsn. contains keratin sulphate, proteoglycan or glycosaminoglycan. Also claimed are compsns. that contain chondroitin or dermatan proteoglycan or glycaosaminoglycan, and mixts. of these. The dermatan sulphate has a C-4 sulphur linkage, and the chondroitin sulphate has a C-6 sulphur linkage. The keratin sulphate may be type I (corneal) or type II (skeletal). Also claimed are compsns. contg. substances that destroy or antagonise the growth inhibiting function of these cpds.. The substances are, e.g., monoclonal antibodies selected from MZ15, 1/20/5-D-4, 4/8/1-B-4, 4-D-1 or 8-C-2, or enzymes such as endo-B-galactosidase, keratinase, chondroitinase or chondroitin ABC lyase.

Also claimed are compsns. contg. heparin or **hyaluronate** disaccharide / proteoglycan / glycosaminoglycan.

USE/ADVANTAGE - The compsns. of keratin sulphate, etc. can inhibit neurite outgrowth, i.e., axonal growth, and glial cell migration or invasion. Studies have shown that heparin inhibits attachment and neurite formation of human neuroblastoma cells on a cholera toxin B/ganglioside GM1-binding substratum (Mungai et al, 1988, Exp. Cell Res. 175-299-247). The enzymes and monoclonal antibodies that antagonise the glycans growth inhibiting ability may be used to reverse nerve damage caused by trauma, surgery, ischaemia, infection, metabolic disease, nutritional deficiency, malignancy, exposure to toxins or degenerative disorders of the nervous system (claimed).

L133 ANSWER 26 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1991-117336 [16] WPIDS
CR 1993-288134 [36]; 1993-288135 [36]; 1998-456173 [39]; 1999-008773 [01]; 1999-610299 [52]; 1999-619695 [53]
DNC C1991-050471
TI **Combinations** of drug and **hyaluronic acid** - to improve tissue and cell penetration.
DC B05 B07 C03 D21
IN ASCULAI, S S; FALK, R E
PA (HYAL-N) HYAL PHARM CORP; (NORP-N) NORPHARMCO INC
CYC 37
PI WO 9104058 A 19910404 (199116)* 116p
RW: AT BE CH DE DK ES FR GB IT LU NL OA SE
W: AT AU BB BG BR CA CH DE DK ES FI GB HU JP KP KR LK LU MC MG MW NL NO RO SD SE SU US
AU 9064330 A 19910418 (199129)
FI 9102470 A 19910521 (199133)
EP 445255 A 19910911 (199137) 116p
R: AT BE CH DE ES FR GB IT LI LU NL SE
ZA 9007564 A 19910828 (199139)
NO 9101952 A 19910705 (199140)
BR 9006924 A 19911210 (199203)
CN 1051503 A 19910522 (199207)
JP 04504579 W 19920813 (199239) 39p A61K047-36
HU 64699 T 19940228 (199412) A61K047-36
AU 9352274 A 19940303 (199414) A61K047-36
WO 9104058 A3 19910919 (199508)
EP 656213 A1 19950607 (199527) EN 116p A61K047-36
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
EP 445255 B1 19951206 (199602) EN 84p A61K047-36
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69024039 E 19960118 (199608) A61K047-36
ES 2080837 T3 19960216 (199614) A61K047-36
AU 674894 B 19970116 (199711) A61K047-36
AU 9714850 A 19970522 (199729) A61K047-36
RO 112812 B1 19980130 (199832) A61K047-36
SG 49658 A1 19980615 (199836) A61K047-36
US 5811410 A 19980922 (199845) A61K031-715
US 5827834 A 19981027 (199850) A61K031-715
US 5830882 A 19981103 (199851) A61K031-715
US 5852002 A 19981222 (199907) A61K031-70
US 5914314 A 19990622 (199931) A61K038-13
US 5929048 A 19990727 (199936) A61K031-70
US 5932560 A 19990803 (199937) A61K031-70
US 5985850 A 19991116 (200001) A61K031-70
US 5985851 A 19991116 (200001) A61K031-715
IL 95745 A 19990922 (200002) A61K047-36
BR 1101180 A3 19991130 (200014) A61K047-36
ADT EP 445255 A EP 1990-914108 19900918; ZA 9007564 A ZA 1990-7564 19900921; JP 04504579 W JP 1990-513204 19900918, WO 1990-CA306 19900918; HU 64699 T HU 1990-7339 19900918, WO 1990-CA306 19900918; AU 9352274 A AU 1993-52274 19931209, Div ex AU 1990-64330 ; WO 9104058 A3 WO 1990-CA306 19900918; EP 656213 A1 EP 1995-100186 19900918; EP 445255 B1 EP 1990-914108 19900918, WO 1990-CA306 19900918; DE 69024039 E DE 1990-624039 19900918, EP 1990-914108 19900918, WO 1990-CA306 19900918; ES 2080837 T3

EP 1990-914108 19900918; AU 674894 B AU 1993-52274 19931209, Div ex AU 1990-64330 ; AU 9714850 A Div ex AU 1993-52274 19931209, AU 1997-14850 19970221; RO 112812 B1 RO 1990-148511 19900918, WO 1990-CA306 19900918; SG 49658 A1 SG 1996-2961 19900918; US 5811410 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1995-465335 19950605; US 5827834 A Cont of WO 1990-CA306 19900918, Cont of US 1991-675908 19910703, US 1994-286263 19940805; US 5830882 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1995-462615 19950605; US 5852002 A Div ex US 1991-675908 19910703, US 1995-462147 19950605; US 5914314 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1995-462614 19950605; US 5929048 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1995-462148 19950605; US 5932560 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1995-461124 19950605; US 5985850 A Div ex WO 1990-CA306 19900918, Div ex US 1990-675908 19910703, US 1995-462154 19950605; US 5985851 A Div ex WO 1990-CA306 19900918, Div ex US 1991-675908 19910703, US 1996-744852 19961118; IL 95745 A IL 1990-95745 19900919; BR 1101180 A3 BR 1997-1101180 19970514

FDT JP 04504579 W Based on WO 9104058; HU 64699 T Based on WO 9104058; EP 445255 B1 Based on WO 9104058; DE 69024039 E Based on EP 445255, Based on WO 9104058; ES 2080837 T3 Based on EP 445255; AU 674894 B Previous Publ. AU 9352274; RO 112812 B1 Based on WO 9104058

PRAI CA 1989-612307 19890921

REP NoSR.Pub; 3.Jnl.Ref; EP 138572; EP 197718; EP 216453; EP 224987; EP 245126; EP 265116; EP 287210; EP 380367; JP 62240628; US 4711780; 02Jnl.Ref

IC ICM A61K031-70; A61K031-715; A61K038-13; A61K047-36
ICS A61K031-34; A61K031-375; A61K031-40; A61K031-72; A61K037-26; A61K047-26; C08B037-00; C08L000-00

ICA C08B037-08

AB WO 9104058 A UPAB: 20000320
New drug combinations or formulations comprise a drug and a **hyaluronic acid** cpd. (I) selected from **hyaluronic acid** and its salts, homologues, analogues, derivs., complexes, esters, fragments and subunits.
USE - Indications include diabetes, hormone replacement therapy, fetility control, AIDS, cancer, hair loss, herpes infections, renal failure, cardiac insufficiency, hypertension, oedema, microbial infections, acne, **transplant** rejection, inflammations, elimination of tumour breakdown material, blood detoxification, respiratory disorders, vascular ischaemia, brain tumours, mononucleosis, pain, side effects of nonsteroidal antiinflammatory agents, and tissue perfusion.
Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: B03-F; B04-B04C5; B04-C02E; B07-A01; B07-D05; B07-D12; **B12-A01**; **B12-A06**; B12-A07; B12-D01; **B12-D02B**; B12-D07; B12-F01B; B12-F05; B12-F07; B12-G03; B12-G04; **B12-G07**; B12-H05; B12-J05; **B12-K02**; B12-K03; B12-K06; B12-L05; C03-F; C04-B04C5; C04-C02E; C07-A01; C07-D05; C07-D12; **C12-A01**; **C12-A06**; C12-A07; C12-D01; **C12-D02B**; C12-D07; C12-F01B; C12-F05; C12-F07; C12-G03; C12-G04; **C12-G07**; C12-H05; C12-J05; **C12-K02**; C12-K03; C12-K06; C12-L05; D06-H; D08-B03

ABEQ EP 445255 B UPAB: 19960115
A pharmaceutical composition comprising: (1) a medicinal and/or therapeutic agent in a therapeutically effective amount to treat a disease or condition in humans; and (2) **hyaluronic acid** and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of **hyaluronic acid**, characterised in that said composition (a) is in a dosage form which is suitable for administration in humans; and (b) is in a form in which (i) component (1) is in an effective dosage amount to treat said disease or condition by penetration at the site to be treated; and (ii) component (2) is immediately available to transport component (1) at the site to be

treated, and which component (2) is in an effective non-toxic amount to facilitate the transport of component (1) upon administration, through the tissue (including scar tissue) at the site to be treated and through the cell membranes of the individual cells to be treated, wherein said amount of component (2) is sufficient to provide a dosage greater than 10 mg/70 kg person.
Dwg.0/1

L133 ANSWER 27 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-149234 [20] WPIDS
CR 1987-362710 [51]; 1991-016249 [03]
DNC C1990-065298
TI Biocompatible, pharmaceutical delivery system - comprises at least one amino polysaccharide selected from chitosonium polymers and **chitosan** derivs..
DC A96 B07
IN BRODE, L; PARTAIN, E M
PA (UNIC) UNION CARBIDE CHEM; (UNIC) UNION CARBIDE CHEM & PLASTICS; (UNIC) UNION CARBIDE CHEM & PLASTICS TECHNOLOGY
CYC 19
PI EP 368253 A 19900516 (199020)* EN 13p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
CA 2002404 A 19900508 (199027)
AU 8944497 A 19900531 (199028)
US 4946870 A 19900807 (199034)
JP 02196728 A 19900803 (199037)
IL 92225 A 19930708 (199335) A61K009-70
KR 9402657 B1 19940328 (199602) A61K009-70
ADT EP 368253 A EP 1989-120624 19891107; US 4946870 A US 1988-268871 19881108; JP 02196728 A JP 1989-288985 19891108; IL 92225 A IL 1989-92225 19891106; KR 9402657 B1 KR 1989-16073 19891107
PRAI US 1988-268871 19881108; US 1986-871381 19860606; US 1988-189312 19880203
REP 4.Jnl.Ref; A3...9139; EP 198246; JP 57180602; JP 61034004; JP 61254517; JP 63010715; US 4365050; WO 8707618
IC A61K009-70; A61K031-71; A61K047-36
ICM A61K009-70
ICS A61K031-71; A61K047-36
AB EP 368253 A UPAB: 19960122
A biocompatible, substantive, film-forming delivery system for the delivery of pharmaceutically or therapeutic activities to a desire topical site of a subject. The system comprises 0.01-99.99 wt% of the total system of at least one aminopolysaccharide selected from chitosonium polymers and chitosan derivs.
USE/ADVANTAGE - The novel delivery systems are useful for the topical delivery of pharmaceutical or therapeutic activities. The system maintains and transmits the necessary amt. of active ingredient to an appropriate site of the body. Chitosan derivs possess a variety of useful characteristics making their materials superior for the delivery of pharmaceutical and therapeutic activities, e.g. film-forming and humectant properties. They are bio-compatible, non-irritant and non-**allergenic**; hence are comfortable to the skin. The compsn. is in the form of a film, a gel, a patch, an aerosol, a suppository, a fibre, a rod microspheres or haemostatic device or soln. The device is selected from pad, sponge, and pref. suture.
0/0
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A09-A; A10-E01; A12-V01; B04-C02E3; **B12-A01**; B12-A07
ABEQ US 4946870 A UPAB: 19930928
New biocompatible substantive topical drug delivery system comprises pharmaceutical and 0.1-99.99% wt.aminopolysaccharide comprising chitosonium polymers and covalent chitosan derivs., in gas-permeable non-irritating film or gel. Aminopolysaccharide may be chitosonium pyrrolidone carboxylate, salicylate, niacinate, lactate, or glycolate and

is pref. blended with **hyaluronic acid**, opt. with diluent. System may be in form of patch, aerosol, suppository, fibre, rod, microspheres, homeostatic device, soln., pad, sponge, suture.
ADVANTAGE - Improved topical delivery system for wide range of pharmaceuticals. @
0/0

L133 ANSWER 28 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1989-206453 [28] WPIDS
CR 1989-206452 [28]
DNC C1989-091672
TI **Topical** compsn. comprising sulphated saccharide - for application to skin or non-gastrointestinal, non-oral, non-bladder mucosa to treat e.g. inflammation, burns, irritation, etc..
DC B03 B04 C02 C03
IN BAR-SHALOM, D; BUKH, N; BARSHALOM, D; BURKH, N
PA (BARS-I) BAR-SHALOM D; (BUKH-N) BUKH MEDITEC AS; (BUKH-N) BUKH MEDITEC A/S; (BUKH-N) BUKH MEDITEK AS
CYC 32
PI WO 8905646 A 19890629 (198928)* EN 43p
RW: AT BE CH DE FR GB IT LU NL OA SE
W: AT AU BB BG BR CH DE DK FI GB HU JP KP KR LK LU MC MG MW NL NO RO SD SE SU US
AU 8929146 A 19890719 (198941)
DK 9001515 A 19900814 (199044)
EP 394333 A 19901031 (199044)
R: AT BE CH DE FR GB IT LI LU NL SE
CA 2020199 A 19911230 (199213)#
JP 04500798 W 19920213 (199213) 16p
DK 9200057 A 19920117 (199229) A61K031-70
AU 9333960 A 19930506 (199325) A61K007-48
KR 9303117 B1 19930419 (199420) A61K031-70
EP 394333 B1 19950315 (199515) EN 10p A61K031-70
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3853365 G 19950420 (199521) A61K031-70
JP 07039347 B2 19950501 (199522) 12p A61K031-70
AU 664419 B 19951116 (199602) A61K007-48
ADT WO 8905646 A WO 1988-DK217 19881221; AU 8929146 A AU 1989-29146 19881221; DK 9001515 A DK 1990-1515 19900621; EP 394333 A EP 1989-901102 19881221; CA 2020199 A CA 1990-2020199 19900629; JP 04500798 W JP 1989-501022 19881221; DK 9200057 A Div ex DK 1990-1515 19881221, DK 1992-57 19920117; AU 9333960 A Div ex AU 1989-29146 19881221, AU 1993-33960 19930303; KR 9303117 B1 WO 1988-DK217 19881221, KR 1989-701562 19890821; EP 394333 B1 WO 1988-DK217 19881221, EP 1989-901102 19881221; DE 3853365 G DE 1988-3853365 19881221, WO 1988-DK217 19881221, EP 1989-901102 19881221; JP 07039347 B2 WO 1988-DK217 19881221, JP 1989-501022 19881221; AU 664419 B Div ex AU 1989-29146 19881221, AU 1993-33960 19930303
FDT EP 394333 B1 Based on WO 8905646; DE 3853365 G Based on EP 394333, Based on WO 8905646; JP 07039347 B2 Based on JP 04500798, Based on WO 8905646; AU 664419 B Previous Publ. AU 9333960
PRAI DK 1987-6740 19871221; DK 1988-5054 19880909; WO 1988-DK217 19881221
REP 2.Jnl.Ref; AU 564201; CA 1218601; EP 107209; EP 136100; EP 230023; JP 59078116; JP 62190127; US 4668665; 1.Jnl.Ref; AT 6588; AU 8432361; CA 1240929; DE 3131811; DE 3376116; EP 130550; EP 136782; EP 245855; EP 254845; EP 63973; FR 2503563; JP 33023389; JP 60056922; JP 63107934; US 4486416; US 4640912; ZA 8703496
IC A61K007-48; A61K031-70; A61L027-00
ICM A61K007-48; A61K031-70
ICS A61K009-00; A61K031-725; A61L027-00
ICA C07H011-00
AB WO 8905646 A UPAB: 19950404
Compsn., partic. for topical applicn. to skin or any non-gastrointestinal, non-oral, non-bladder mucosal surface comprises a sulphated saccharide (I) or salt or complex, with an acceptable carrier or excipient. A non-sulphated polysaccharide eg **hyaluronic acid**, may

also be present.
USE - Used for preventing or treating non-bladder premalignant or malignant disorders; for preventing or treating irritation or burns of the skin, connective tissue or non-oral mucosa; for preventing or treating skin, connective tissue or mucosal ageing; or for preventing or treating infectious, malignant or **allergic**/ immune disorders (all claimed).
(I) may be used in tissue culture media (claimed) and for coating eg. catheters to reduce thrombus formation or prevent inflammatory responses.
Dwg.0/0
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C02; B07-A02; B10-A07; **B12-A01**; **B12-A06**; **B12-D02**; B12-D07; **B12-G07**; B12-H02; B12-M02F; C04-C02; C07-A02; C10-A07; **C12-A01**; **C12-A06**; **C12-D02**; C12-D07; **C12-G07**; C12-H02; C12-M02F
ABEQ EP 394333 B UPAB: 19950425
Use of sulphated mono- or disaccharide or a salt or complex thereof for combatting or preventing ageing of skin, including treating or preventing skin wrinkles.
Dwg.0/0

L133 ANSWER 29 OF 29 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1987-009251 [02] WPIDS
DNC C1987-003525
TI **Medical use** of glycosaminoglycan cpds. - for treating connective tissue diseases.
DC B04
IN CHOAY, J; HORNBECK, W; PETITOU, M; ROBERT, L
PA (LCHO) DROPIC; (SNFI) SANOFI SA
CYC 12
PI EP 208623 A 19870114 (198702)* FR 34p
R: AT BE CH DE FR GB IT LI LU NL SE
FR 2584606 A 19870116 (198708)
JP 62018401 A 19870127 (198709)
ADT EP 208623 A EP 1986-401562 19860711; FR 2584606 A FR 1985-10788 19850712; JP 62018401 A JP 1986-163490 19860711
PRAI FR 1985-10788 19850712
REP 8.Jnl.Ref; A3...9001; EP 138572; EP 140781; EP 143393; EP 27089; EP 37319; FR 2440376; FR 2461719; FR 2503714; No-SR.Pub; US 4141973
IC A61K031-72; C08B037-08
AB EP 208623 A UPAB: 19930922
Use of glycosaminoglycans (GAG) and/or GAG fragments, opt. in salt form, for prodn. of medicaments for treating connective tissue diseases is new.
Specified GAG include heparin, heparin sulphate, heparin fragments such as those described in FR2440376, 2461719, 2478646, 2572080 and 2504928, dermatan sulphate, chondroitin, chondroitin sulphate and **hyaluronic acid**. The GAG are formulated as injectable solns. with a conc. of 1-200 (esp. 20-150)mg/ml for s.c. admin. or 30-100 (esp. 40-50)mg/ml for i.v. admin. or perfusion.
USE/ADVANTAGE - GAG may be used to treat cardiovascular, osteo-articular and pulmonary disorders associated with ageing, as well as inflammatory conditions and malignant tumours. They selectively inhibit elastase activity and are practically free of side effects.
0/4
FS CPI
FA AB
MC CPI: B04-B02C3; B04-B04G; B04-C02E; B12-B04; B12-C01; B12-C05; B12-D07; B12-E01; B12-F01; B12-G01; B12-G01B3; **B12-G07**; **B12-J08**; B12-K06; B12-N01; **D05-H**